JANUARY, 1931.

BRAIN.

PART 4, VOL. 53.

DISSEMINATED SCLEROSIS IN NORTH WALES.

AN INQUIRY INTO ITS INCIDENCE, FREQUENCY, DISTRIBUTION AND OTHER ÆTIOLOGICAL FACTORS.

[This work was done with the aid of a grant from the Medical Research Council.]

BY R. S. ALLISON, M.D., M.R.C.P.

I.—INTRODUCTION.

THE first to describe a case of disseminated sclerosis in this country was Moxon. To-day, though much is known of the symptoms, histology and morbid anatomy of the disease, the ætiology and pathogenesis are still obscure. In the latter half of the nineteenth and early part of the present century, histories of cases were collected and analysed and such factors as shock, injury, infectious diseases and intoxications related to the onset of symptoms. Since the war, interest in this subject has been revived, probably stimulated by the experiments with animals and attempts to pass on the disease begun by Bulloch in 1913. Papers have been published at home and abroad which suggest that disseminated sclerosis has a selective geographic incidence; that it occurs with greatest frequency in country districts, and in the occupations of farming and wood-working. It should be noted, however, that these conclusions are based, for the most part, on statistical evidence. There is, perhaps, a danger that they may be too readily accepted and influence opinion without first being submitted to closer scrutiny. Indeed, many of the authors concerned, notably Adams, McAlpine, Steiner and Dana, have suggested that it would be advisable to survey given areas or districts for cases of disseminated sclerosis. In this way the mode of living and habits of individual patients could be studied, and the results compared with those of statistical methods on a larger scale. It is possible, too, that by these means a common factor might be discovered which would throw some light on the vexed problem of ætiology.

Though the subject has been approached since then, so far as the writer is aware no work has actually been done on these lines. The

idea is attractive, but it is clear that it can only be applied on a small scale in the first instance, if a personal investigation is made of each case. Later, if thought desirable, more extensive surveys could be arranged by a group of workers acting over a larger field. For the single worker the area selected should be small and well defined. In forming conclusions, prevailing local conditions are apt to be a source of error in a small district. This can, however, be avoided by contrasting the living conditions of affected cases with those of the rest of the inhabitants.

With these objects in view, this work was begun in the autumn of 1928. The district selected was North Wales, where the writer was living. This seemed a suitable area to explore. It is well defined and many of the inhabitants live in small secluded towns or isolated farmhouses, the conditions of life offering much variety and scope for comparison. The expenses incurred were covered by a grant from the Medical Research Council, to whom the project was referred in the first instance.

II.—Description of the Area surveyed.

(*a*) *Size, divisions, geographic features.*—The province of North Wales consists of the counties of Denbigh, Flint, Caernarvon, Anglesey and Merioneth. The total area is approximately 2,430 square miles, and the relative sizes of the various counties may be judged from the accompanying Map (fig. 1).

Anglesey is an island having an undulating surface close to sea level. The land is rocky and marshy in places and for the most part given over to agriculture. Lead and copper deposits are worked at Amlwch. The climate is humid but mild.

Flint is composed of a plateau rising about 500 to 800 ft. above sea level, and is dry and fertile for agriculture and rich in mineral deposits (coal and lead). Low-lying districts are situated at the mouth of the River Clwyd and along the shores of the Dee estuary (Prestatyn, Flint).

Denbigh has an irregular surface, consisting in parts of bleak hills and moorland with small lakes. The fertile Vale of Clwyd however is rich in pasture land. The climate here is mild and comparatively dry. Indeed Rhyl is said to hold the record among seaside resorts in England and Wales for sunshine. The industrial area round Wrexham is rich in minerals. The county is on the whole well wooded and possesses

a fair amount of arable land, whilst on the upland farms sheep are reared.

Caernarvon and Merioneth may be considered together as their central portions are occupied by a solid block of mountain ranges

FIG. 1.

separated by deep and secluded valleys. There are numerous lakes, the largest being Bala Lake in Merioneth, about four miles long. Arable land is confined to the valleys, coastal areas and Nevin Peninsula, and

sheep and cattle raising occupy the attention of most farmers. The climate is damp and cold in winter.

(*b*) *Population, occupation, rural and urban distribution.*—At the 1921 census the population of the five counties was 489,270 inhabitants, distributed as follows :[1]—

County	Urban districts	Rural districts	Total
Denbigh ..	56,002 ..	98,845 ..	154,847
Caernarvon ..	68,281 ..	62,694 ..	130,975
Flint ..	43,224 ..	63,393 ..	106,617
Anglesey ..	19,789 ..	31,955 ..	51,744
Merioneth ..	20,255 ..	24,832 ..	45,087
	207,551 (42 per cent.)	281,719 (58 per cent.)	489,270

It is interesting to note that only 58 per cent. of the total inhabitants live in rural districts and 42 per cent. in urban. A higher proportion of rural dwellers would have been expected in such an essentially country district. This is accounted for, however, by the geographic features of Caernarvon and Merioneth. Here, the inhabitants are grouped together in small towns, large tracts of moorland and mountainous country being practically uninhabited. The other counties, and particularly Anglesey, show a strong proportion of rural dwellers as might be expected from their natural features.

There are no cities or large towns, the largest town being Colwyn Bay with 21,566 inhabitants. Other towns of smaller size are Llandudno, Wrexham, Rhyl, Bangor, Holyhead, Blaenau Festiniog and Caernarvon (8,340).

The chief occupation of the province is farming and in the mountainous districts slate quarrying is followed on a large scale particularly in the towns of Blaenau Festiniog and Bethesda. In parts of Flint and Denbigh there are coal mines ; brick, iron and chemical works notably in Wrexham, Buckley, Mold, Hawarden, Flint. Except for these there are no other important industries. Along the coast there are many summer resorts and schools. In these, a number of the inhabitants follow occupations connected with the summer influx of visitors and teaching.

III.—The Methods employed.

(*a*) *Collection of cases.*—The cases were collected through the courtesy of the medical men in practice in North Wales, to whom the writer is deeply indebted for their friendly and sympathetic help. It

[1] Information obtained from the County Educational Authorities and Annual Reports of County M.O.H.'s.

was felt that patients could scarcely pass through all phases of the disease without seeking medical advice and the local doctor was the most likely to be first consulted. Disseminated sclerosis is a rare disease in general medical practice. If not recognized as such, the serious nature of the symptoms would prompt the doctor to seek help at the nearest hospital centre. In this way, the cases in his district, if any, would be known to him.

From the current medical directory a list of doctors practising in North Wales was drawn up. A letter was then sent to each doctor with stamped envelope and form suitable for reply. The letter briefly set out the object aimed at and asked for information of cases. It was requested that not only should typical established cases be reported but also doubtful or early cases showing one or more of the signs and symptoms associated with the disease. An address was given on the objects of the work at a meeting of the North Wales Branch of the British Medical Association in May, 1929. There was a large attendance and much enthusiasm was raised.

Success, of course, depended entirely on the willingness with which the doctors in practice would co-operate with the objects of the inquiry. Considerable doubt was felt at first on this score, but the results obtained proved this doubt to be entirely unworthy. By the autumn of 1929 replies had been received from practically all the doctors (266 out of 273). This was a sufficient testimony to the willingness of practitioners to help with the research and to indicate that more information relating to the incidence of disease in general might usefully be obtained in this way.

(*b*) *Collection of information relating to cases.*—After notification a suitable day and time were arranged with the doctor concerned and the case visited in his company. Patients were seen at their homes. If the disease had begun elsewhere, so far as possible this place was also visited. Ample time was given to each case to obtain a careful history, make an examination and inspect the living conditions. It was seldom possible to investigate more than one case at a time. As a rule the doctor and responsible relatives were present at the interview. Statements made by the patient could thus be confirmed and supplemented. Without exception, the patients and their relatives gave every help and welcomed rather than discouraged the inquiry.

Altogether 125 cases were reported, 65 of these being cases of disseminated sclerosis. Six of these had been treated in Ruthin Castle during the past five years. The remaining 61 were doubtful cases, or

examples of other diseases of the nervous system, such as encephalitis lethargica, neurosyphilis, &c. As a rule the replies from doctors stated that they had no cases in their practice, or that they had one typical case and two or three doubtful ones, presenting one or more of the signs of disseminated sclerosis. It often happened too that when a visit was paid to a district, the writer was asked to see other cases of nervous disease. These doubtful and extra cases were purposely included in the total so that they should serve as controls to the true cases when required. In this way the large number of extra cases reported is accounted for.

The 126 cases were classified as follows:—

Class A.	Typical cases of disseminated sclerosis	= 39
,, *B.*	Early cases in which disseminated sclerosis was a probable diagnosis	= 10
,, *C.*	Histories of cases deceased or untraceable	= 16
,, *D.*	Doubtful cases, symptoms and signs inconclusive	= 9
,, *E.*	Examples of other diseases of nervous system	= 52
		126

With one or two exceptions and excluding Class *C*, the above cases were investigated personally by the writer.

History-taking and examination.—The same routine procedure was followed in all cases. The plan was as follows:—

(1) *Family history.*—Cause of death or state of health of parents and brothers and sisters. Place in the family. Direct inquiry for paralysis, fits, insanity, nervous breakdowns, in other members of the family.

(2) *Injury, shock, exposure.*—Date and relation to onset and course of symptoms. Character.

(3) *Occupation.*—Nature and conditions under which work was done. If more than one occupation had been followed, dates of change noted. Spare time pursuits and hobbies. Leading questions regarding work with wood, animals, agriculture.

(4) *Pregnancy, menses, marriage.*—Age of onset and character of menstruation; menopause. Civil state at onset disease. Effect of confinements on onset and course.

(5) *History of life.*—Place of birth, occupation of parents and early living conditions. Dwelling places in town or country. Accommodation, water supply, sanitation, geographic features. Living conditions at onset of disease inspected for above points. Leading questions, *re* premises infested with rats, damp and cold, contact with animals, farm work, insect bites.

(6) *History of illness.*—Date and character of onset. Remissions and exacerbations. March of symptoms.

(7) *Examination.*—Build and stature. Fair or dark type. Mentality, cranial nerves, motor and sensory functions, reflexes, state of spine and joints. Result of blood Wassermann and examination of cerebro-spinal fluid.

In some the information available was scanty and unreliable, but in many others every facility was afforded for an accurate survey of the habits and living conditions. Much of the data sought was probably irrelevant but it was felt that the inquiry should be as full as possible as a unique opportunity was offered of seeing these patients in their own environment. It is usually difficult to obtain accurate information about family history and previous illnesses from the hospital patient. The patient may be willing enough but his memory will not serve. In this inquiry the help of the family doctor and relatives of the patient was invaluable, and much which otherwise would have been lost is recorded.

The onset of the disease in each case was fixed as accurately as possible. This is a difficult task, especially in cases of long standing. Usually it could be traced back before the date given by the patient. This uncertainty about the onset is admittedly a weak point in relating conditions of life to it. If the habits or circumstances of a person render him liable to develop disseminated sclerosis, it is important that we should be able to fix the date of onset fairly closely. It was a fortunate thing therefore that a number of the patients had lived in the same place and under the same conditions for some years before and after the earliest symptom.

Diagnosis presented difficulty in many cases. So far as possible doubtful cases were excluded and only those with typical features were put in Class *A*. A big proportion had been in hospital and the diagnosis already made and supplemented by examination of the cerebrospinal fluid. For obvious reasons lumbar puncture was not practicable, but in those cases where it had not already been done the blood was taken and the Wassermann reaction performed.

In the following chapters, devoted to the various aspects of the aetiology, the literature is first discussed and then an analysis made of the information collected from the cases. The results are compared with what is already known, and conclusions are drawn.

Chapter I.—Age, Sex and Civil State.

Age.—The age of onset of the disease was noted in fifty-nine of the cases of disseminated sclerosis. This was found to be in accord with the already well-established opinion that it is most common between the ages of 20 to 40. Birley and Dudgeon found in their series of thirty-five cases that the average age of onset was 24·6 years and according to

Collin and Baehr, 88 per cent. of their cases began before the thirty-fifth year. Gowers stated that the disease is met with at all periods of life and especially in the first half of adult life, the majority of cases beginning between the ages of 20 to 35. Below is given a table showing the experience of several writers and including the present work. A graph (fig. 2) has been drawn from these figures and it will be seen that this supports Gowers' contention.

Author	No. cases	0–10	10–20	20–30	30–40	40–50	50–60	60–70
Bing and Reese	272	—	13	92	99	41	20	7
Wechsler ..	194	1	11	65	72	36	8	1
Jelliffe ..	105	9	8	21	27	20	19	1
Present work ..	59	—	6	28	19	4	2	
Morawitz ..	33	—	7	14	10	21	—	
Girones ..	10	—	1	6	3	—	—	—
	673	10	46	226	230	122	49	9

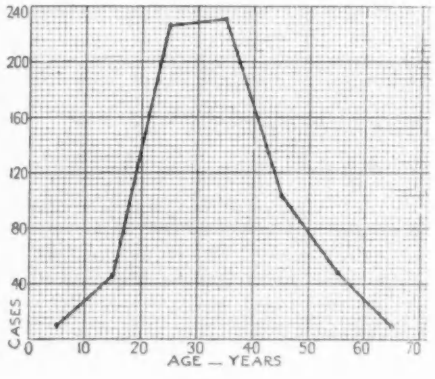

FIG. 2.

Sex.—The opinion generally held is that sex has no moment. When small numbers of cases are collected, as a rule one sex predominates. Thus in Girones' 10 cases, there were 8 females and 2 males. Of the 35 cases of Birley and Dudgeon, there were 23 females and 12 males. Blumreich and Jacoby found 23 males and 6 females in 29 cases. Of 60 patients collected in North Wales, 20 were males and 40 females. When larger numbers are considered, it is clear that the disease is fairly evenly distributed between the sexes. To illustrate the truth of this, a total of 4,808 cases has been selected from the literature of various countries. This shows that 2,373 were males and 2,435 females, a proportion of about half and half.

Author	Country	Cases	Males	Females
Wilson	England and Wales	688	343	345
Grainger Stewart ..	England	1,920	790	1,130
Adams and Blackrock ..	Scotland ..	14	11	3
Foster Coates	Ireland	100	61	39
Present work	Wales	60	20	40
Blumreich and Jacoby ..	Germany ..	29	23	6
Morawitz	Germany ..	33	15	18
Klausner	Germany ..	126	78	48
Dreyfuss	Germany ..	1,151	672	479
Krafft-Ebing	Germany ..	100	58	42
Bing and Reese	Switzerland ..	281	117	164
Jelliffe	America	109	68	41
Wechsler	America	197	117	80
		4,808	2,373	2,425

Civil state.—Wechsler commented on the absence of statistics on this subject. He found in 186 cases that 63·5 per cent. were married and 36·5 per cent. single. There is no indication whether this referred to their state at the time of examination or at the onset of the disease. Presumably it was the former. This point was noted in 56 of my cases. Thirty-five (62·5 per cent.) were single and 21 (37·5 per cent.) were married at the onset. Taken later at the time of examination, as a result of more marriages, the married proportion was raised to 47 per cent. approximately. In only one case was the onset closely related to marriage. In this (Mrs. Pl.), marriage had been advised for a supposed neurosis, in reality the early symptoms of the disease which were unrecognized until afterwards.

Conclusions.

(1) In the majority of cases the disease begins between the ages of 20 and 35.

(2) Men and women are equally liable to develop the disease.

(3) In this series of cases, more single than married persons were affected.

Chapter II.—Menstruation, Climacteric, Parturition.

It is well known that the first symptoms of disseminated sclerosis sometimes begin after parturition. It was thought advisable, therefore, to inquire into the menstrual and child-bearing history of the female patients, to discover if there was any connection between these and the onset of the disease.

Menstruation.—The menstrual history was obtained in 26 cases. In 21, the periods were regular, normal in amount, duration and in the

amount of discomfort felt. In 5 cases the following notes were made:—

Case 14*a*.—Sarah J. Menses began at age of 18 to 19 and have always been infrequent and scanty. The onset of the disease was at age of 31.

Case 27*a*.—Mrs. Rob. Before marriage at age of 25 menses were unduly frequent and the loss heavy. After marriage they became normal in character. Onset at age of 28.

Case 37*a*.—Mrs. Wr. Up till marriage severe dysmenorrhœa with prostration, pre-menstrual abdominal colic and vomiting. Onset at age of 11 or 12.

Case 28*a*.—Bella R. Menses irregular, infrequent and scanty until onset of illness at age of 30. Since then they have been normal.

Case 10*b*.—Jenny W. Menstruation began at age of 13, periods irregular at first, in a year or so became normal. Onset of illness at age of 13 about same time as beginning of menstruation.

The climacteric.—The change of life has an effect on the health of many women who tend to develop functional nervous disorders, high blood-pressure, &c., at this time. This point was considered in six of the 34 female cases who had passed the menopause. In three of these the onset of first symptoms bore some time relation to it.

Case 7*a*.—Mrs. El., aged 50. Onset of D.S. four years ago, with sudden blindness and recovery. Recurrence of symptoms a year ago. Periods irregular for past two years, now ceased at age of 54.

Case 34*a*.—Mrs. Und. Symptoms of menopause, i.e., flushings, irregular periods with final stoppage in 1917-18, aged 54. In 1918, after influenza, noticed first symptom of present disease (D.S.)

Case 24*a*.—Mrs. Pr. Onset of D.S. at age of 40. Since then relapses and remissions. Menses normal till age of 44 when had severe menorrhagia. In view of this an artificial menopause was produced with radium at age of 45.

Parturition.—Of 22 married women in this series, 14 had borne children. Parturition had been related either to the onset or to a relapse occurring during the course of the disease in 8. In the remaining 6 it had been uneventful.

(1) *Parturition related to Onset.*

Case 31*a*.—Mrs. Sut. Married at 20. Two years later a son was born. A month or so after this she noticed a weakness of the legs and stiffness (onset). As this occurred over twenty years ago the patient could not be more accurate.

Case 27*a*.—Mrs. Rob. Married at age of 25. No children by design, till became pregnant three years later. Patient states that the present complaint began shortly after this child was born. Labour was conducted under "twilight sleep" and was very successful from an obstetric point of view. The doctor

naturally wondered if this process had been harmful and in any way connected with the onset of D.S. The husband, however, recollected what the patient herself had forgotten, that during the early months of pregnancy she had complained of pins and needles in the right arm and leg. These were disregarded until after parturition, when they became more noticeable and were accompanied by weakness of the right leg.

Case 15*a*.—Mrs. Jo. Married at age of 19. A year later a child was born without ill-effects. At age of 24 a second child was born. Shortly after, unsteadiness in walking was noticed and she fell downstairs. She was also very emotional and her husband thought her hysterical. Recovery took place in a month or two. Four years later, when aged 28, a third child was born. Six weeks after parturition weakness of the legs was felt, the speech was indistinct and vision blurred. The patient, her husband and the doctor who attended her throughout are all positive that symptoms did not appear until after childbirth on each occasion.

Case 30*a*.—Mrs. Sp. Married at age of 26. A child was born one and two years after marriage. No ill-effects were observed, but both children proved weakly and died shortly after birth. Aged 30, four years after marriage, gave birth to a third child. A week after parturition had a bad fright (husband became insane) and she noticed weakness of the right leg with stiffness.

Case 9*b*.—Mrs. Wil. Married at age of 22. Has had six children, two of whom are alive to-day, two died in infancy and two were stillborn. The last child was born fifteen years ago, when patient aged 41. Labour was precipitate, the child being born before the arrival of the doctor. There had been no ill-effects after the previous confinements and pregnancy in this last instance was uneventful. Shortly after parturition (two to four weeks) noticed weakness of the legs, particularly of the right.

Case 19*a*.—Mrs. Mat. Married at the age of 28. A year later gave birth to a healthy child. The first symptoms of the present illness were noticed during pregnancy in a mild form and more severely after parturition. They consisted of "pins and needles" in the right leg with weakness and dragging of the right leg (onset).

(2) *Parturition related to Relapses.*

Case 23*a*.—Mrs. Pl. Was single when illness began with sudden blindness at age of 35. Married at age of 36. Three years ago gave birth to a healthy child. During pregnancy her symptoms were less, but after parturition she became worse. She is now pregnant again, and this time is worse rather than better, with retention of urine and paraplegia.

Case 10*a*.—Mrs. Hu. Married at age of 25. Two years later noticed weakness of right leg, which, however, passed off. Aged 32, a son was born, and shortly after this suffered from incontinence of urine and precipitate micturition. This recovered and at age of 40 gave birth to another child. During the puerperium noticed that the sight was blurred and indistinct and that the right leg felt weak.

Parturition causing no Ill-effects.

Case 37*a*.—Mrs. Wr. First symptom noticed at age of 11; next at age of 19. Married at age of 22. A child was born a year later, the labour being easy. A second child was born two and a half years after the first, aged 25-26. There was phlebitis of the left leg after this, but no other ill-effects. Neither confinement or pregnancy had any effects on the course of the disease. This did not become chronic and fully established till some years after the birth of the children.

Case 7*c*.—Mrs. Jo. Married at age of 22. Onset of D.S. at age of 27. Two children were born before she was 27 and two since then. Three are living to-day and one is dead. Neither the confinements nor the pregnancies had any ill-effect.

Case 16*a*.—Mrs. Lew. Married at 19. She has seven healthy children, aged 26, 25, 23, 21, 15, 9, 7. The present illness began at age of 34, half way through her child-bearing period between the fifth and sixth children. It was unconnected with parturition and the subsequent pregnancies had no noticeable effect on its course or severity.

Case 7*a*.—Mrs. El. Has been married for over twenty years. Has six children and had two miscarriages. Three children are alive and healthy, the other three died in infancy. All the children were born some years before onset of D.S. at age of 50, four years ago. No transitory symptoms were observed at any of the confinements or pregnancies.

Case 34*a*.—Mrs. Und. Married at age of 28. Has two healthy children, aged 30 and 28. Noticed no nervous symptoms before or after birth of these. Onset of D.S. at age of 55, some years after last confinement.

Case 24*a*.—Mrs. Pr. Married at age of 24. A child was born a year later; now alive and well. Noticed no nervous symptoms before or after birth. Onset of D.S. occurred at age of 40, many years later.

Summary and Discussion.

(1) *Menstruation.*—This was normal in the majority, in only two out of twenty-six was there a history of scanty and irregular periods. Of twenty-two married women, fourteen had borne children. These facts suggest that there was no defect in their ovarian secretion. There appeared to be no time relation between the onset of the disease and the beginning and cessation of menstruation. This had begun some years before the disseminated sclerosis in all but one case. In this one exception both had started in the same year, and in only three cases was the onset related to the climacteric.

(2) *Pregnancy and parturition.*—Fourteen patients had borne children. No ill-effects were observed in six, but in eight, that is more than half, pregnancy and parturition were related either to the onset or to a relapse in the course of the disease. In some, the first symptoms

were noticed during pregnancy, and in others not until after the birth of the child. The history of Mrs. Rob. suggests that often the first symptoms are unnoticed during pregnancy, and that the disease may be present in latent form before the birth of the child. This is in keeping with the statement of some of those patients who became pregnant after the disease had begun. They noticed that during pregnancy they tended to feel better, but felt worse after delivery. There was no history of difficult labour and the children born were usually healthy.

It is obvious that child-bearing cannot be of first ætiological importance. It can only apply to women, and even so, only a proportion of those who bore children were affected. Also it should be noted that in three cases symptoms followed, not after the birth of the first child, but after the second, third and sixth child respectively. This suggests that some other factor had been added in the interval which had not been present previously. The effects of pregnancy and parturition therefore appear to be auxillary in unmasking a latent condition. This takes place most frequently after parturition, during the puerperium, when the general physical state of the patient may be low.

Chapter III.—Injury, Shock and Fatigue, Exposure.

These three causes have been grouped together for convenience as they are very similar and are probably the commonest causes given by patients to explain the onset of their symptoms. Leuba is stated to have been the first to note the frequent connection between injury and the onset of disseminated sclerosis. Blumreich and Jacoby, in a careful study of twenty-nine cases, found a history of injury related to the onset in eleven. In nine others there was a history of overwork or shock. Krafft-Ebing found a history of exposure to extremes of temperature in forty out of 100 cases, and concluded that this was an important ætiological factor. Thus one case cited by him was that of a young woman who developed the disease shortly after spending thirty minutes in a cold bath in the month of October! Numerous cases have been described where an accident seemed related to the onset; amongst these may be mentioned the cases of Baldwin, Palmer, Pemberton and Grossmann. Jordan reported a case after an emotional shock; Preissner, another, is a man who had been struck by lightning. The European War of 1914-18 should have furnished numerous examples following injury, shock and exposure, had these factors been important, but in

reality records of such cases are rare. Josephy collected thirty-seven cases in soldiers, but found that only in four was there any connection between the onset and an injury received. In only two of these was the connection at all likely.

It is generally agreed to-day, that neither injury, shock nor exposure have any real value as causes of the disease. Grainger Stewart states that it is inconceivable that the pathological changes characteristic of the disease should result from the direct effects of an injury, and he believes that exposure and fatigue probably act in accentuating already existing conditions.

Fifty-six cases of disseminated sclerosis were investigated from this standpoint. The patients were first asked if they could name any likely cause for their illness. If unable to do so, they were questioned about former injury, exposure, shock and fatigue. To act as a control to these results, forty patients who had some other affection of the nervous system were examined in a similar way. The results are tabulated below :—

INJURY—EXPOSURE—SHOCK.

Class.	Number of cases.	Injury given as cause	Previous injury not given as cause	Exposure given as cause	History of exposure not given as cause	Shock given as cause	Over fatigue given as cause	Total	
D.S. (*A, B, C*)	56	8	6	3	5	1	1	24	43
Controls (*D, E*)	40	6	4	1	6	1	1	19	47

From the above figures it is obvious that injury, shock and exposure occur as antecedents in disseminated sclerosis with no greater frequency than in other diseases of the nervous system. In fact, in this series of cases, drawn from the same area and more or less living under the same conditions, these factors were rather less frequently met with in disseminated sclerosis than in other diseases. Personal investigation, combined with the help of relatives under ideal conditions, no doubt accounts for the high figures obtained. It is of interest to note that whereas exposure was given as a cause only four out of fifteen times, injury was cited as a cause in fourteen out of twenty-four instances. This difference is no doubt related to the weighty impression which an injury makes on the mind of an individual as compared to such everyday occurrences as exposure to damp and wet.

In the fourteen cases of disseminated sclerosis giving a history of previous injury, an attempt was made to find out what bearing, if any,

this had on the subsequent onset and course of symptoms. The cases were found to fall readily into three groups, and some examples of each are given.

(A) Injury some time before Onset of Symptoms.

Case 25a.—Isac P. At age of 20 was cycling, when his machine skidded and he was thrown violently into a shallow pond of icy-cold water. He was shaken, and felt as if a tight band were round the abdomen, but walked home, a distance of 1½ miles. X-ray is said to have shown a fracture of the spine and the sensation of tightness after persisting for some months was relieved by massage. He kept well till five years later, when at age of 25 the symptoms of disseminated sclerosis first appeared.

This suggests an injury to spinal cord with root pains five years before the onset of symptoms. On examination, there was no evidence of localization of symptoms at site of old injury or signs of compression of cord.

Case 6a.—Alan E. Whilst in army, aged 36, fell over a gun limber and broke the left leg. Two years later noticed first symptom of present illness (D.S.), i.e., weakness of the left leg with dragging.

This suggests that the site of a former injury may determine the site of onset of symptoms. The same feature was observed in another case, Robert Jones.

(B) Injury closely related to Onset of Symptoms.

Case 2a.—John A. At age of 20, was walking one stormy night in March on outskirts of Barmouth. Rain and wind being severe, he sheltered under a wall. Whilst there, he was aware of a sudden flash and a bang, and found himself lying on the road, his left leg being twisted under him. On getting up, he found that a chimney on a nearby house had collapsed, damaging the wall he was sheltering under, in its fall. He concluded that he had been struck by lightning. No one else had noticed thunder or lightning that night, and the patient himself admitted that it was the only "bang" and flash he had been aware of. He was badly shaken. His left leg felt numb and weak, though he was able to walk. A few weeks later he had "influenza," which recurred in a month, and after the second attack he noticed double vision and dragging of the left leg. He is now an established case of D.S., and believes that his illness is due to being struck by lightning.

It appears likely that there was no lightning, and that the chimney collapsed owing to the force of the wind. Probably he was knocked down by part of the wall falling on him. The left leg was twisted in the fall. The weakness noticed at the time was not out of proportion to the injury. His illness was ushered in some weeks later by febrile attacks and malaise, described as "influenza." It is more probable that the onset of the disease was related to these attacks, and that its appearance after the injury was purely a coincidence.

Case 1a.—Mrs. Al. Aged 43, received a shock whilst adjusting some wires leading to an electric light bulb. The next morning she noticed numbness in

the right leg, and a week later had lost the use of the limb. She believes that this was the beginning of her present illness (advanced D.S.), and that it was caused by the electric shock received. On closer inquiry it was found that three months previous to the above events she had been very emotional and depressed, and had had violent tremors of the right arm on attempted movement. Many years before, when aged 22, she had had a bad nervous breakdown following influenza, with weakness of the legs which persisted for several weeks.

(3) *Case* of Rudolf H. described by Grossmann. Grossmann first saw this patient in April, 1905. He showed signs of well-established D.S. and stated that his symptoms had followed closely on an accident in October, 1903, when he had fallen from a height and been taken to hospital unconscious. The man's comrades testified that he had been in excellent health and able for hard work before the accident. Hoping to find a bona-fide case of post-traumatic disseminated sclerosis, Grossmann looked up the original hospital records. He found notes of an examination made a few days after the accident, viz., optic atrophy, nystagmus, intention tremor, forced laughing and unequal knee-jerks. The author concludes that it would have been impossible for such advanced signs to have developed in a few days.

The conclusion seems justified that this patient was suffering from the disease in a latent, though advanced form. His faculties were not impaired until after the accident, which served to unmask the latent disease.

(C) Injury a Result rather than a Cause.

(There were numerous examples of this.)

Case 24a.—Mrs. Und. In October, 1919, when out walking, slipped and fell on asphalt pavement, injuring the right knee. After this accident she noticed that the legs felt weak and she dates her illness from it.

On inquiry it was found that in August, 1919, the patient was lame in the left leg for a month or so.

It is probable that the patient fell because her legs were weak and that the injury resulted from weakness of the legs rather than the reverse which she alleged.

Conclusions.

(1) A history of injury, shock or exposure was often met with in the fifty-six cases of disseminated sclerosis examined, but not more frequently than in a control series of forty cases of other diseases of the nervous system.

(2) In some cases, where a part had been injured some time before the onset of symptoms, the disease appeared to affect the function of that part first.

(3) In other cases there was a close connection between an injury

and the first recognition of symptoms. Though often given causal value by patients this apparent relation is more probably due to :—

(*a*) Forgetfulness on the part of the patients of earlier symptoms.

(*b*) The injury being the result rather than the cause of symptoms.

(*c*) The disease being present in latent unrecognized form before the injury, the latter serving to draw attention to it.

(*d*) Coincidence.

Chapter IV.—The Influence of Heredity.

Formerly, disseminated sclerosis was considered by many to be a primary degenerative process. Thus Strümpell thought it was a multiple gliosis dependent on congenital influences. Müller was of the same opinion, being unable to find an external cause in the majority of his cases. In modern times, one of the few remaining advocates of the older view is Hassin. After a careful examination of pathological material from thirteen cases, this worker came to the conclusion that the essential cause was a degeneration of myelin and that there was no evidence of an inflammatory process.

From the standpoint of ætiology, it is clear that if the disease is a primary degeneration, search for external causes will not be of much value. At the most, such effects could only be contributory or secondary. A primary degeneration suggests a congenitally weak or unstable nervous system. The causes of this are more likely to be found in the family history of the patient. One might expect frequent instances of the disease in members of the same family, an early age of onset and a neuropathic inheritance. Furthermore, it might be possible to recognize certain distinctive physical types as being especially liable to develop the disease. The present series of cases was investigated along these lines.

Familial Incidence.

The number of familial cases reported in the literature is small. Eichhorst, Reynolds, Batten, Allen, Robinson and Abrahamson have contributed examples. The cases described by Eichhorst in 1896 and 1913 were confirmed by autopsy. They are probably the most convincing in the literature. A brief summary of them is given below :—

(1896).—Case of a woman with weakness of legs, tremor, scanning speech, nystagmus and pallor of discs. Two years after onset a son was born who subsequently developed similar symptoms. At autopsy, in each case, small sclerotic patches were found scattered throughout the spinal cord.

(1913).—Mother and son with symptoms of spastic paraplegia. At autopsy, grey patches varying in size were found in the brain and spinal cord.

Many writers, notably Cestan and Guillain, Ferguson and Critchley, have described familial diseases closely resembling disseminated sclerosis. The last-named authors described a family in which thirteen members were affected, the clinical picture varying from that of paralysis agitans to disseminated sclerosis. The inference is that many familial diseases, which are certainly not disseminated sclerosis, closely mimic it in their clinical features. For this reason many of the so-called familial cases, which were formerly accepted and lent support to the hereditary view, are now discredited.

Only four cases were reported in North Wales. Two of these were in a brother and sister. The sister's case was obscure and had at one time been diagnosed as disseminated sclerosis. *Case* 13*c*.—Barbara H. On examination it appeared more probable that the condition was due to the after-effects of encephalitis lethargica. The brother (*Case* D(5), William H.) showed a spastic paraplegia, and syphilis had been excluded. Two more probable cases were found in sisters. On clinical grounds these presented typical features of disseminated sclerosis. One of them was living in North Wales and was examined personally. The main features are given below. Except for these two no other familial cases were found in North Wales.

Case 32*a*.—Bessie T., aged 43 (examined personally). At age of 18 sudden blindness left eye and right vision blurred, recovering completely in right eye, only partially in left. Aged 30, noticed left foot dragging and sensation "as if a cat were rubbing his back against the leg." This lasted one to two months. Aged 32, had nervous breakdown, apprehensive and emotional. At age of 35, lameness left leg which has persisted since and has spread to other leg and to the left arm. *On examination*: temporal fields of vision reduced with pallor of discs. Intention tremor right and left. Spastic paraplegia, right greater than left. Tendon reflexes +, ankle clonus and extensor plantars, absent abdominals. Difficulty in retaining urine and constipation. Wassermann reaction negative.

Case 14*c*.—Nellie T., aged 41 (from notes). At age of 23, "neuritis" in left arm. Aged 32 numbness of legs, the right one being weak. Treated n Guy's Hospital. Wassermann reaction negative in blood and C.S.F. Diagnosis of disseminated sclerosis. Recovered partially but at age of 35 lost control of bladder. Admitted Liverpool Royal Infirmary—cranial nerves normal, no

speech defect or intention tremor. Knee-jerks +++, ankle and patellar clonus, extensor plantars, absent abdominal reflexes. Recovered and kept well till age of 38, when both legs affected with weakness. Since then has been a semi-invalid.

Early Age of Onset.

Strümpell and Oppenheim believed that the disease could be traced in its beginnings to early childhood. If so, this would strengthen the primary degenerative view and bring the disease into line with other congenital affections. Recently Wechsler has made an excellent review of the subject and concludes that the majority of so-called cases in children are based on insufficient evidence; that such cases are in reality often examples of other diseases, such as Friedreich's ataxia, congenital lues, Little's disease, family spastic paralysis and the after-effects of encephalitis lethargica. In his own series of 197 cases he found only four in children. He concluded, therefore, that whereas undoubted cases do occasionally occur in childhood, such are extremely rare.

It is difficult to decide what may be the first symptom in a given instance. For example, in No. 37*a*, Mrs. Wr., of this series, there was transient numbness of the left leg at the age of 11, and not till 19 was the next symptom, temporary blindness, noticed. If the plan is adopted of noting all possible nervous symptoms from childhood onwards, full justice will be done to the theory of beginning in early life. In fifty cases it was possible to do this fairly closely. The judges of former fitness were the family doctor, the parents, brothers and sisters. In forty-two (84 per cent.) the patients appeared to have been in robust physical and mental health until the onset in adult life. In only eight (16 per cent.) was there a history of nervous symptoms in childhood. In only two could the onset be fairly placed before the age of 15. Details are given below:—

Case 29*a*.—Joseph R. Always nervous and sensitive. Stammering a feature of early life. Onset at age of 26.

Case 37*a*.—Mrs. Wr. Aged 11 noticed numbness of the left leg, which lasted one week. Did not do anything about this, and was otherwise well till aged 19, when became temporarily blind (onset).

Case 5*a*.—Winifred E. As a child was always unduly sensitive; "felt things more than others." Was shy, conscientious and hard worker. Onset at age of 30.

Case 14*a*.—Sarah J. As a child and up till onset in adult life always "delicate," readily tired by exertion, over-sensitive and unduly apprehensive.

Case 20*a*.—Marjorie O. Parents state she was the most "nervous" child of the family. Was always "highly strung," very sensitive and kept her own

company. Easily frightened and shy of strangers. Strong physically. Onset at age of 20.

Case 5*b*.—Nesta R. As a child was always nervous, readily frightened, shy and over-conscientious. Onset at age of 23.

Case 21*a*.—Cassie O. Always unduly sensitive, more reserved and shy than other members of the family. Physically strong. Onset at 20.

Case 10*b*.—Jenny W. From earliest childhood shy and sensitive. Robust physically. Aged 13 noticed diplopia and weakness left side of face (onset).

Neuropathic Inheritance.

Gowers held that an indirect neuropathic inheritance was fairly common in disseminated sclerosis. Krafft-Ebing found seventeen out of 100 cases in which the family history showed drunkenness, insanity, migraine and other examples of nervous disease. Steiner, on the contrary, believes that nervous and mental diseases are no more common in the relatives of cases of disseminated sclerosis than in those of healthy individuals.

In forty cases the family history was investigated closely. In fourteen (35 per cent.) there was a history of nervous or mental disease in other members of the same family.

Case 34*a*.—Mrs. Und. Father died of apoplexy and two brothers were alcoholics.

Case 37*a*.—Mrs. Wr. One brother suffered from severe shell-shock during war.

Case 4*a*.—Mrs. Bar. One sister has had nervous breakdowns and is of a highly excitable type. Her daughter (niece of patient) has had melancholia, now recovered.

Case 24*a*.—Mrs. Pr. Two first cousins affected; the one with a temporary paraplegia lasting a year (? disseminated sclerosis), the other with a nervous breakdown.

Case 20*a*.—Marjorie O. Paternal grandfather died of apoplexy, maternal grandfather of paralysis agitans; an aunt suffers from fits.

Case 5*a*.—Winifred E. Mother hemiplegic as result of several strokes.

Case 29*a*.—Joseph R. One sister neurasthenic; had chorea as a child. Another sister died from melancholia, "refused food and withered away" (? anorexia nervosa).

Case 21*a*.—Cassie O. One brother an epileptic; fourteen in family, patient thirteenth; last child died infancy.

Case 9*a*.—John H. One sister suffers from neurasthenia.

Case 7*a*.—Mrs. El. One brother died tabes dorsalis.

Case 10*a*.—Mrs. Hu. Father died of apoplexy. One sister has weakness in the legs from time to time. All brothers and sisters "very highly strung."

Case 32*a*. Bessie T. One brother an epileptic. One sister symptoms suggestive of disseminated sclerosis.

Case 22*a*.—Jane O. Father died aged 71, "very nervous." One brother suffers from periodic depression. One sister is melancholic.

Case 2*c*.—Mother suffers from paralysis agitans.

Type of Person affected.

Charles Dana states that he has never seen a case in an obese subject and Davenport suggests that it is the tall northern or Scandinavian races in America who appear to be most liable.

Notes were made in these cases of the physical characteristics, whether tall or short in stature, bodily nutrition at the time of onset and whether the patients were of the dark or fair haired type.

Height.—In 47 cases, 33 were of average height, 10 were tall in stature (women over 5 ft. 8 in., men 6 ft. or over) and 4 were below average height. Thus, in this series, persons of average height were most commonly affected, but tall individuals were twice as common as short ones.

Nutrition.—In 46 cases, 24 were of average nutrition, 20 undernourished and of the "asthenic" type and 2 obese. Undernutrition was therefore unduly prevalent at the time of onset and obesity rarely found.

Type.—In 47 cases, 33 belonged to the dark haired and complexioned type and 14 to the fair haired type, the dark types outnumbering the fair by about 2 : 1. Dark types are however commonly met with in North Wales.

Place in family.—In 34 cases, the birth relation to other brothers and sisters was noted. In only 1 case was the patient an only child. Four were the eldest and 6 the youngest members of their respective families. Eight belonged to the first half and 19 to the second half. The only point of note is therefore the apparent tendency in this series of the younger or more junior members of large families to be affected.

Summary and Comments.

(1) *Familial incidence*.—Authentic records of familial cases are rare. Only two examples in sisters were found among sixty-five cases.

(2) *Alleged early onset*.—The majority of so-called cases in children are not disseminated sclerosis. In only two cases in this series did the disease begin in childhood. In the great majority, there were no

nervous symptoms of any kind, until the onset in adult life, the persons affected having been previously healthy subjects.

(3) *Neuropathic inheritance.*—Nervous and mental diseases were found in the families of 14 out of 40 cases (35 per cent.), the former 10 times and the latter 15 times.

(4) *Special physical type.*—No one type was found but the disease appears to be more common in thin persons, and dark types outnumbered the fair by 2 to 1. This latter proportion, however, is probably true of the district as a whole. Tallness of stature was twice as common as shortness. Of 34 cases, 18 were among the last born in their respective families and 8 among the first born.

There is little, therefore, on ætiological grounds, to support the view that disseminated sclerosis is due to a primary degeneration dependent on congenital hereditary influences. Instances of its occurrence in families are rare and its beginnings cannot be traced to early life. It appears however that those who are affected with the disease frequently come from families which show a liability to nervous and mental disease in general. This, of course, is no more than may be said of many other diseases, both infective and degenerative, which show the same tendency to run in families.

Chapter V.—Racial and Geographic Distribution.

Disseminated sclerosis is not a notifiable disease, and it is therefore not possible to obtain exact information of its incidence in the general population. Wilson found, however, that in 1925, 688 persons died from the disease in England and Wales. Steiner believes that after neurosyphilis disseminated sclerosis is the commonest organic disease of the nervous system. Through hospital returns one can assess its frequency among other diseases. Thus Williamson found that during ten years at the Manchester Royal Infirmary 2,294 cases of nervous disease of all kinds were treated, and that of these 61 were disseminated sclerosis (2·7 per cent.). Grainger Stewart was able to collect information of 1,920 cases from the records of the National Hospital, Queen's Square, where only nervous diseases are treated; 10 per cent. of the annual admissions were disseminated sclerosis.

The geographic and racial distribution of the disease has for long been a subject of discussion. What evidence there is points to a selective rather than a free distribution of the disease throughout the world. The work which has been done on these lines will now be discussed.

(*a*) *Racial Distribution.*

(1) *Infrequency of disseminated sclerosis in America.*—Early in the present century the suggestion was made that the disease was more common in Europe than in America. Thus in 1903 Bramwell concluded, from a comparison of his own cases with those of contemporary American writers, that it was three and a half times more common in England than in America. Among 2,760 hospital patients with general nervous diseases he found 1·8 per cent. cases of disseminated sclerosis. Jelliffe, on the other hand, among 21,502 cases found only 104 or a rate of 0·3 per cent. These figures are typical of those given at this period. Collins and Baehr, writing in 1914, referred to the possibility that the apparent infrequency in America was due, not so much to rarity, as to differences in diagnostic criteria, many cases being labelled disseminated sclerosis in Europe which would not be so called in America. It is to be noted, however, that their findings of only 91 out of 12,000 cases (0·75 per cent.) supported the general contention.

Light has been thrown on this subject more recently from a different angle. Pearce Bailey has written an interesting paper on disseminated sclerosis in American military recruits during the war. A total number of 6,916 cases of organic nervous disease was reported, and of these 511 had disseminated sclerosis. The rate for disseminated sclerosis among nervous diseases as a whole, functional and organic, was 0·74 per cent., almost the same as Collins and Baehr's figure. "The average of foreign-born (Europeans) in the whole group of organic conditions was 9·2 per cent., while in multiple sclerosis it was higher, 12·7." This seems to indicate that the disease is less common in native-born Americans than in Europeans. It is of interest to note here that Jelliffe, writing nineteen years before, found among his 109 patients that more than half were European-born.

(2) *Frequency in Europe.*—The greater part of the literature on disseminated sclerosis has been contributed by France, Germany and Great Britain. The large bulk of this is in itself evidence in favour of the frequency of the disease in these countries. Monrad-Krohn states that it is common in Norway. In 1926 Bing and Reese published the results of a survey of north-west Switzerland for disseminated sclerosis. They collected 950 cases and calculated that this would give a rate of 1 in 3 or 4,000 of the population. These results have suggested to some that the disease is especially prevalent in Switzerland. Before this conclusion is drawn it should be remembered that we have nothing

of a similar kind with which to compare these results. The present investigation in North Wales is, however, directed along similar lines. Excluding the six cases from Ruthin Castle and two from Liverpool there remain 57 (in Classes A, B and C) which were found in this area which has a population of 489,270. This gives a rate of about 1 case per 8,600 of the inhabitants. The writer's feeling is that this number is probably an under-estimate. Adams has found disseminated sclerosis a common organic disease of the nervous system in the West of Scotland, and Foster Coates has referred to its frequency in the North of Ireland. He found 106 out of 728 cases of nervous disease treated in the Royal Victoria Hospital, Belfast, in three years (14·5 per cent.). This is the highest rate which has been recorded

American writers have been able to draw reasonable conclusions as to its relative frequency among the various European races. Thus Pearce Bailey, already referred to, found among his foreign-born recruits that disseminated sclerosis was most frequent in Scandinavians (12·5), in French next (10·7), Slavs (9), Germans (8·3), Scotch (8·2), English (8·1) and Irish (7·9). In the other races the incidence was much lower. These results have been supported by Davenport, who noted the birthplace of seventy foreign-born cases in New York. He found that the English and Germans had about twice as many cases as might be expected, the Irish slightly more and Scandinavians three times the number. The Italians were far below expectations. Jelliffe also found that among his foreign-born patients Germans and British predominated.

(3) *Frequency in eastern and tropical countries.*—Steiner states that a South American neurologist informed him that the disease is rare in that continent. Miura, speaking at a German Congress in 1911, commented on the few cases he had met with in Japan. Sprawson, who worked in India for twenty-seven years, had not seen a single case in a native, though he had come across two cases in Europeans resident in India. This experience, however, was not shared by some of the other speakers at the conference where the discussion took place.

(4) *Distribution of cases in explored areas.*—In no part of the world does disseminated sclerosis occur endemically, and it is difficult to draw conclusions about the natural conditions under which it is most liable to develop. Davenport made a map of the United States to show the incidence of it in the various States. This was based on knowledge of the homes of military recruits, rejected on account of the disease. He found that cases occurred with greatest frequency in the States of

Minnesota, Michigan and Wisconsin. He noted that these States bordered on the great lakes and are inhabited largely by Scandinavians and their descendants. Bing and Reese also published a map of north-west Switzerland plotting the cases found on it. There was nothing remarkable about the result. Wilson noted the place of death of 688 persons who had died from the disease in 1926 in England and Wales. The maximum incidence was found to be in Peterboro', Merioneth, Monmouth, Cardigan and Cornwall. These are mainly rural districts, and except the first named have a sea coast. The writer has been unable to substantiate the claims of Merionethshire. He found the disease in this county not more frequent than in the others.

In this work, the cases found in North Wales were plotted on a large-scale map, a black dot representing each case. The number charted was forty-seven, the remaining cases having to be omitted for various reasons. In forty the disease began and the patients lived within the confines of North Wales. Six cases occurred in the Wrexham area, four near Bala in Merioneth, along the valley of the river Dee, and five in the coastal area around Llandudno and Colwyn Bay. There was no congregation at any one point. Except for the Bala district the other parts have a fairly dense population, and are places where, in the ordinary course, one might expect to meet with a fair number of cases. Ten cases occurred in Anglesey. This seems a large number for a small area and thinly-populated county. The population of Anglesey forms about 10 per cent. of the total for North Wales, whereas 25 per cent. of the forty cases were found there. This frequency in Anglesey is not due to any special facilities for investigation there. Indeed, as it was the most distant part from the centre of the inquiry, it was the least accessible. It is probable that the number of cases found there is an underestimate. This finding may or may not be related to the geographic features of the county, Anglesey being a flat open country with no part much raised above sea level.

Summary and Comments.

Though cases have been reported from recognized centres all over the world, Europe appears to be chiefly affected, and particularly Great Britain, France, Germany, Scandinavia and Switzerland. The disease is less common in North America than in Europe. What little is known suggests that it is rare in tropical and Eastern countries. It may be said, therefore, to occur most frequently in northern latitudes and temperate climates. In North Wales cases were found scattered along

the lines of thickest population, but Anglesey, which is a low-lying, flat open district, had a larger proportion than might have been expected. The rate found was about 1 in 8,600 inhabitants.

Chapter VI.—Rural and Urban Incidence.

Is disseminated sclerosis more common in country districts than in towns and cities? Several observers have recorded their impressions. Grainger Stewart believes that the disease is met with as frequently in industrial and urban areas as in rural districts. Müller found that most of his cases (from Strümpell's Clinic) came from the country and Morawitz, working at Tübingen, found that it was the commonest disease of the nervous system in the Würtemberg country district. Steiner thinks that it is much more a disease of the country than of the town, and that when it occurs in town dwellers inquiry will often show that they formerly lived on the land. Adams is a supporter of the same view, and finds that the majority of his patients come from the country as opposed to the town.

These views show that there is a strong bias in favour of the country incidence. It will be observed, however, that individual impressions are apt to be coloured by the nature of the district in which they are made. Granted that disseminated sclerosis is probably one of the commonest organic nervous diseases in the country, we require further evidence to prove that the disease is actually more frequent there than in towns. Recourse must be had to the method of investigating a given area if this point is to be decided. The total population and the ratio of urban to rural dwellers should be known. By contrasting the dwelling-places of the cases found with these facts a true estimate can be formed of the distribution of the disease in the area. Some work has already been done on these lines and in this study the same method has been adopted.

In the United States C. B. Davenport found a defect rate for disseminated sclerosis among recruits of 10 in 100,000 of the population examined. The urban rate was 12 in 100,000 and the rural 8 in 100,000. He concluded, therefore, that the urban rate for the disease was one-half greater than the rural rate.

In Northern Ireland Foster Coates collected 100 cases from the records of the Royal Victoria Hospital, Belfast. He found that two-thirds were town and one-third country dwellers. Now 10 per cent. only of the general hospital population came from the country. This suggested that the disease was more common in the country. On

looking over these figures, however, it is difficult to escape from the fact that two-thirds of his cases were town dwellers.

Bing and Reese in a survey of north-west Switzerland found the largest rate (7·4 in 10,000 inhabitants) in Basel City. On examining the excellent tables given one is struck by the small rate for cases in areas of small population—presumably rural areas. The greatest rate appears to be in the more thickly-populated areas. The author's only comment on this point was that the greater frequency of the disease in Basel may have been due to the improved facilities for diagnosis existing in cities as compared to country districts. The Swiss results certainly do not indicate that the disease is unduly prevalent in rural districts.

Else Koch in a recent paper has noted the place of birth and dwelling of 700 German military war pensioners invalided because of the disease. Figures were given which showed the distribution of the German population over urban and rural areas. By "rural" was meant districts having a population of under 2,000 inhabitants. From these figures it is evident that approximately 45 per cent. of the total population may be classified as rural and 55 per cent. as urban. Koch found that 425 of the pensioners (60 per cent.) were born in rural and 275 (40 per cent.) in urban districts. This showed a preponderance in favour of the country for birth-place. When the dwelling-places of the 700 pensioners were considered it was found, however, that more came from towns than from the country (301 rural, 43 per cent., and 379 urban, 57 per cent.). Though Koch attributes this to the tendency of the population to migrate to cities in recent years, and evidently believes that the disease is essentially a rural one, there appears to be little to support her contention from the above figures.

In investigating the subject of rural and urban incidence in North Wales forty-five cases were available. The same plan of noting the birth and dwelling place was followed, and in addition the place of onset was noted.

Place of Birth.

Twenty-five cases were born in the country or in villages, whilst twenty were born in towns, cities or industrial areas.

Persons born in country or village	=	25 cases
,, ,, industrial areas and small towns	=	5 ,,
,, ,, large towns or cities	=	15 ,,

Places lived in during Life.

Though there was a small number who had moved about from place to place, the majority of patients had spent all their life either in towns

or in the country. Special inquiry was directed towards ascertaining whether or not the patients had at any time lived or worked on a farm or in the country. The results were as follows :—

Persons who had always lived in the country or on farms ..	=	20 cases
,, ,, always lived in towns or industrial areas and had never worked or lived in country or farm	=	17 ,,
,, ,, lived both in town and in country ..	=	8 ,,

The country dwellers predominated; 28-45 (62 per cent.). Nevertheless the number of patients who had always lived in towns is striking and the difference between the two groups is not great.

Place of Onset of Disease.

In determining the place of onset of the disease, it was an advantage that in this series of cases thirty-seven out of the forty-five investigated had always lived in either town or country and many always in the same place. In a few the onset had followed shortly after a change of dwelling. These were omitted to avoid confusion.

Persons living in country or in a village at onset	=	25 cases
,, ,, towns at time of onset	=	20 ,,

Thus after considering the places of birth, dwelling-places and sites of onset, there is no indication that the disease occurs more commonly in country dwellers than in town dwellers. The distribution between urban and rural districts is approximately equal with a slight preponderance in favour of the country. This corresponds closely to the distribution of the population as a whole in the area investigated.

SUMMARY.

	Urban	Rural
Place of birth	44 per cent.	56 per cent.
Dwelling place	38 ,, ,,	62 ,, ,,
Onset	44 ,, ,,	56 ,, ,,
General population	42 ,, ,,	58 ,, ,,

It is clear that the distribution of disseminated sclerosis in North Wales closely follows that of the general population. There is no evidence to suggest that it is more commonly met with in the country than in towns and industrial areas. This conclusion appears to be in keeping with that of other workers who have adopted similar methods of inquiry.

Judging from the statements of doctors in practice the disease does not appear to be unduly prevalent in the province. The majority have seen one or two cases at some time or another, but a number deny its existence in their districts entirely. A large number said that they had

found encephalitis lethargica and its after-affects a more common disease. At a rough estimate, had this inquiry concerned the latter, 100 to 150 cases might have been collected. Neurosyphilis appears to be as uncommon here as in other rural areas.

Chapter VII.—Occupation.

Literature.

(1) *Industrial causes.*—The possibility that occupation might have some connection with the ætiology of disseminated sclerosis was originally suggested by Oppenheim. He found the disease common in lead, copper and phosphorus workers, in engravers, lithographers, and those working with aniline dyes. Oppenheim's views, however, have not received general support and the opinion of most writers to-day is that metallic poisoning plays little or no part in the ætiology of the disease. McGurn reported two cases in young men following carbon monoxide poisoning. The first showed, three and a half years after exposure, scanning speech, nystagmus, failing vision, exaggerated tendon jerks, ankle clonus and extensor plantar responses. In this case there was a convincing relationship between the exposure to CO fumes and the onset of symptoms. The description of the second case raises doubt as to the diagnosis. Recently, Helpert described a case following CO poisoning and has given a good review of the literature bearing on this subject. Such examples are undoubtedly rare.

(2) *Farming and agricultural work.*—Hoffman found a large proportion of his cases, 37 to 100, among farm workers, but concluded that the type of occupation depended largely on the local conditions surrounding the hospital or clinic where the observations were made. Adams finds that the occupations most common in his patients are farming, wood-working, game-keeping, gardening and byre-keeping. Foster Coates analysed the occupations of 100 hospital patients in Northern Ireland. He found 17 labourers, 19 household workers and 10 farmers. The percentage of farmers in the general hospital population was 3 per cent. and he concluded therefore that the 10 per cent. farmers found in disseminated sclerosis pointed to a prevalence of this occupation in the disease. Wilson investigated the occupations of 688 persons who had died in England and Wales in 1925. After classifying the occupations, the actual number of deaths in a given occupation were compared with the expected deaths. Farmers, for example, in whom the expected death-rate was 7·46, showed an actual

death-rate of 16, a difference of 8·54. None of the other occupations showed a greater variance between expected and actual deaths than 3 at the most. The total number of deaths in farmers, farm labourers and their relatives or dependants was 56, not a large proportion of the 688, but nevertheless the greatest number of deaths in any one occupation recorded. Bing and Reese, in their survey of Switzerland, noted the occupations of 281 persons; 29 were factory workers, 27 agricultural workers and 110 were engaged in household duties. Industries and trades outnumbered agricultural workers by 52 to 27. They were therefore unable to support the alleged frequency of the disease in farmers and agricultural workers.

(3) *Wood-workers.*—The most comprehensive work on the subject of occupation has been done by three German workers, Dreyfuss, Barnass and Koch. In 1921, Dreyfuss collected 1,151 cases (648 from the literature) and found a preponderance for rural occupations (Landwirtschaftberufe). He admitted in all fairness, however, that this finding was not of much value in itself, as in most countries the number of persons engaged in rural occupations is usually high; 672 of the cases were manual workers and he went into this question more closely. The frequency of a given occupation in 1,000 of the population was contrasted with the frequency of a given occupation in 1,000 cases of disseminated sclerosis. By this method he found a preponderance in favour of joiners and cabinet makers (+ 7·8). This was the highest figure noted in a long series of occupations given. Tailors were + 5·7 and painters + 5·4. The frequency in tailors is explained on the possibility that this occupation, requiring less physical effort, may be taken up on the appearance of early signs of the disease. The same reasoning, however, cannot be applied to painters! Dreyfuss divided the manual workers into three classes: wood-workers, metal-workers and building trades. By the same comparative method, he found an overwhelming preponderance in favour of wood-workers (+ 21·3), the building trades being + 12 and the metal-workers − 36·3. Barnass and Koch's conclusions in finding a frequency in wood-workers are very similar. Like Dreyfuss, they were unable to conduct a personal investigation but relied on the information supplied by the pensions papers of 700 military invalids suffering from the disease.

Present Work.

The occupations of 58 persons suffering from disseminated sclerosis were investigated. The total number of cases is too small to draw

direct conclusions from, and some consideration must be given to the general frequency of various occupations in the district. Some comparative method was necessary to find out if there was any true frequency of the disease in certain occupations more than in others. The method adopted was to compare these results with the occupations found in 40 other "control" cases living in North Wales. It was thus possible to contrast the frequency of various occupations in the two groups and decide if any particular one occurred with greater frequency in disseminated sclerosis than in other diseases.

Many of the patients gave more than one occupation. Thus, *Case 9a*, John H., had been a grocer's assistant until 1914. He had served in the war as a soldier and returned afterwards to work in a slate quarry. His illness began when he was in the army. Some patients followed two or more occupations simultaneously. Thus, *Case 4b*, Lloyd J., was a builder by trade but lived and worked on a farm and mended boots and shoes in his spare time. It was not possible to differentiate between these various occupations and decide which was important and which not. All were recorded so that they should have their full significance.

The results are set out in the accompanying table. In column (1) the various occupations (83) followed during the course of the lives of 58 cases of disseminated sclerosis are noted. In column (2) the same procedure is adopted for the 40 controls (57 occupations). In column (3) the occupations (60) pursued at the time of onset of disseminated sclerosis are noted.

Occupation	(1) Various occupations followed during life. 58 cases D.S.	(2) Various occupations followed during life. 40 cases "controls"	(3) Actual occupation at onset. 58 cases D.S.
Domestic work	29	24	18
Agricultural work (farmers, gardeners, labourers, &c.)	12	11	8
Teaching	8	4	3
Shop workers	7	5	7
Soldiers	6	2	3
Clerical workers (clerks, typists, secretaries, &c.)	5	1	5
Hotel and restaurant workers ..	4	1	3
Quarrymen	4	2	5
Factory workers	2	0	5
Building trades	2	2	1
Students and pupils	4	4	2

Domestic workers head the list. This is of no special significance when taken into account with the preponderance of females in the series of cases.

Land-workers formed about 14 per cent. of the various occupations given in disseminated sclerosis (12 out of 83) and about 19 per cent. of the occupations of the control cases (11 out of 57). 13 per cent. had been working on the land at the time of onset of the disease. These figures do not suggest that farmers as a class are more prone to develop disseminated sclerosis than other diseases of the nervous system. In the report of the Medical Officer of Health for the County of Caernarvon it is stated that 7,965 of the male population of 45,249 were engaged in agricultural work. This works out at about 18 per cent. and closely corresponds to the above figures.

Teachers.—Eight times out of 83 (about 10 per cent.) represents the frequency of this occupation in disseminated sclerosis and 4 times out of 57 (7 per cent.) in the controls. This suggests a prevalence of disseminated sclerosis among teachers but it should be noted that only 5 per cent. were actually employed in this work at the time of onset of the disease. Again, teaching is a fairly common occupation in North Wales on account of the large number of schools in the area.

Clerical workers.—Five out of the 83 occupations given in disseminated sclerosis were clerical (6 per cent.) At the onset of the disease the number was 5 in 60 (8 per cent.); in the controls clerical work was mentioned once in 57 times (2 per cent.). In Caernarvonshire, approximately 2·3 per cent. of the population is engaged in clerical work. There is some evidence here, therefore, to suggest that clerical workers are more prone to develop the disease.

Wood-workers.—In view of the attention which has been given to this subject special inquiry was made for work with wood in all cases. Only one case occurred however in the whole series (*Case* 10 *c*, Stephen J., a joiner).

Other occupations.—These showed nothing of significance and tended to follow the general distribution of occupation in the population as compared with the controls.

Summary and Comments.

(1) A comparative study has been made of the occupations of fifty-eight cases of disseminated sclerosis and forty cases of other diseases of the nervous system found in North Wales.

(2) No evidence has been found to show that the disease is unduly prevalent in wood-workers or farmers, or more commonly met with in the agricultural classes than are other diseases of the nervous system.

(3) The occupations of teaching and clerical work were noted to be more common than might be expected.

Chapter VIII.—Living Conditions.

The work under this heading was divided into three portions :—

(1) To search for cases occurring in the same house, village, town or district.

(2) To inquire for certain alleged factors.

(3) To inspect the living conditions of the cases found.

(1) *Cases occurring together.*—In the sixty-five cases investigated none were found living in the same house, street or district. In some of the towns such as Mold, Holywell and Colwyn Bay, two to three cases were reported, but this had no significance. The patients had migrated from other places widely apart after the disease had begun. A case was seen in Ponkey, near Wrexham (*A* 15, Mrs. Jo.) and shortly after another obscure nervous disease was reported living next door (*E* 35, William S.). On examination however this was thought to be probably encephalitis lethargica, and the hope of finding adjoining cases of disseminated sclerosis had to be abandoned.

(2) *Inquiry for certain alleged factors.*—Steiner found a history of insect bite and particularly tick-bite in many cases and believes this to be of importance. Ticks appear to be more common on the continent of Europe than in the United Kingdom, judging from the statements of farmers. Though most sheep and other animals such as dogs and cattle may harbour ticks in their wool or hair, farm workers in this country are not often bitten. Only two gave a history of insect bite. Wilson suggests the rat as a possible source of infection and found a history of bathing, immersion or working in rat-polluted water in many of the persons examined by her. In deference to this view leading questions were put to forty-five cases of disseminated sclerosis (Classes *A* and *B*) concerning rats. Positive replies were received from only thirteen and nine of these were farm workers who were likely to meet with the vermin in the course of their work. The usual statement was rat-infested dwelling house or farm premises with a few instances of polluted water supply.

This finding may be compared with the control cases. Similar questions were put to forty persons in Classes *D* and *E*. A positive history of living in contact with rats was obtained in twelve.

(3) *Living conditions.*—It was felt that only those patients who had spent their lives in one place or under the same conditions were suitable for investigation. It is probable that little is to be gained from a study of those who have moved from place to place and lived under

varying conditions. Nothing short of a life history would suffice, and even then the difficulty would arise of deciding what was important and what was not. In North Wales, only ten cases of disseminated sclerosis were found which answered to these requirements. These persons had dwelt in the same house or district before and after the onset of the disease, often in small isolated communities, where the conditions were simple and relatively easy to study. These places were visited and inspected, and the information obtained supplemented by the patient's doctor or relatives. The following points were noted:—

(1) Natural features of the neighbourhood.
(2) Type of house, subsoil, accommodation, sanitation.
(3) Water supply.
(4) Routine of life and work.

Case A 7.—Mrs. El. Has lived in the same house in a small town on the sea coast of Anglesey for twenty-six years. Indoor life. Housework. Good house. Water supply from a shallow open well on the cliffs nearby. On the hillside, about 10 to 15 yards above the well, is a large stagnant pool of rain water, no doubt supplying the well by filtration.

Case A 8.—Mrs. Fl. Was born and has lived all her life at present address in small town in an industrial district in Flintshire. Good terrace house. Water supply from town mains. Father and brothers coal miners, and husband a fitter in engineering works. Housework, and lives mostly indoors.

Case A 12.—Price J. Born and lived all his life in a village in Carnarvonshire, situated in an inland valley enclosed by mountains. Large cottage type of house, part shop. Dry sanitation. Water supply by mains from small reservoir in hills. Formerly from well. At onset of illness worked as slate quarryman.

Case A 21.—Cassie O. Born and lived all life in same house in a sea-coast village in Anglesey. House almost on seashore in exposed situation, well built. The water supply is peculiar in that the house has its own well under the floor of the backyard. The other houses in the village are supplied with tap water from the mains. Housework.

Case A 38.—Alex. W. Has lived in Llandudno in same house for twenty years. It is a small cottage wedged in between others in a back street behind a large hotel on sea front. Interior naturally dark and damp, rooms small and badly ventilated. Water supply from town mains. Labourer on odd jobs in town.

Case A 39.—Owen W. For past seventeen years has lived with parents in a cottage in the country of Anglesey, standing by itself in a marshy flat pastural inland district. Well built. Dry sanitation. Water supply from a shallow open well nearby. Works as labourer.

Case B 1.—Elias H. Was born and has always lived in the same place, a village in Carnarvonshire, situated inland high up on a mountain side. Small

terrace house in exposed situation. Well built, dry sanitation and good water from a mountain spring.

Case B 4.—Lloyd J. Lifelong residence on a farm in Denbighshire, situated in an island district on a hillside and on dry rocky ground. The house is large, built of stone and dry. Water supply is unsatisfactory. It is obtained from a well placed under the floor of the kitchen. It is thus liable to be fouled from the farmyard where pigs, cattle and sheep congregate. Works on farm in summer and is a builder's plasterer.

Case B 5.—Nesta R. Born and always lived in a small town in an industrial area near Wrexham. The house is well built of brick and dry. Water supply from mains. Housework, most of time indoors.

Case B 6.—Kathleen S. Born and has lived with her parents on a farm in Denbighshire, situated on a hillside bordering a narrow inland valley. House built of stone and in good repair. Dry sanitation. Water supply from a well. School teacher.

Though the cases selected had a common factor in always having lived in the same place the resemblance ends there. The histories show that the disease may begin in persons living near the sea, in inland mountain valleys, open country districts, towns or industrial areas. The type of house ranged from humble cottage in the country or back street to a large house or villa. Some had spent their lives mostly indoors, others had worked in the open.

The remaining fifty-five cases had moved from one place to another. Points of interest are noted below:—

Case A 16.—Mrs. Lew. Farmer's wife. Present illness began in 1915-16. At that time had been living on a farm in Merionethshire for nine years. Water was from a shallow well in the farmyard and often tasted peculiar. The present occupants who were interviewed state that the water has often a fatty scum and that the dead bodies of rats have been noticed in the well which is not properly covered. The well is close to the house in the farmyard and is almost certainly contaminated from the yard and a nearby duck pond.

Case A 23.—Mrs. Pl. A few months before onset of present illness came to work as governess in village in Northamptonshire. The water supply was bad. Her employers and the other servants drank bottled aerated water or boiled the local supply. She was careless and often drank the water and noticed that it had a brackish taste. The water came in pipes from an open stagnant pool or small reservoir nearby. These statements were not confirmed.

Case A 27.—Mrs. Rob. Lived in London till three years before onset present illness, when married and moved to a village in Denbighshire. The sanitation was faulty, the terrace in which she lived being drained by a cesspool placed in the back garden. This overflowed and fouled the land and was later closed by order of the M.O.H. Confirmed.

Case B 9.—Mrs. Wil. Has lived at present address for twenty years. Small cottage in coastal village in Anglesey. The walls are damp and water collects on the floor. Water from a public well of old-fashioned type in village.

The only recurring feature in these cases seems to have been an unsatisfactory water supply, generally obtained from wells which were liable to pollution. In thirty-five control cases (Classes *D* and *E*) details of the water supply were also noted. Water was obtained from a main supply by pipes in twenty-three and from private wells in eleven. It is an interesting fact, when taken into consideration with the above, that in only one case (*E*. 32, Mrs. Rob.) was the water supply stated to be unsatisfactory.

Summary and Comments.

(1) No instance was noted of two or more cases having lived together in the same house, town or district. Such examples are probably rare. The rule is to find cases scattered over a wide area, one in this village, another in that town, and so on.

(2) Contact with rats and tick-bites were found in some cases but not with any special frequency when compared with the control cases of other diseases of the nervous system.

(3) The majority of cases had moved about from place to place. Ten were found, however, who had lived in the same house or district most, if not all, of their lives. In these the environment and habits were noted. In the remainder a search was made for common circumstances. The only recurring feature was an unsatisfactory water supply. In most cases this was derived from a well, which was in such a position as to be subject to animal pollution.

Synopsis.

The main object of this work was to note the frequency and distribution of disseminated sclerosis in North Wales, and to inquire into the occupations and living conditions of affected persons. At the same time it was found convenient to study the subjects of age, sex, injury, exposure, pregnancy and heredity. The conclusions reached are in accord with what is already known concerning these events in their relation to the onset of the disease.

The method adopted, of working through the doctors in practice in the district, was most satisfactory. The total number of cases, however, was too small to be of much value in forming direct conclu-

sions. This difficulty was partly overcome by comparing them with a series of control cases of other diseases of the nervous system, taken from the same area and similarly investigated. Diagnosis presented another difficulty as post-mortem evidence was lacking. Of the total 65 cases, 39 were typical clinical examples, 10 were early cases in which disseminated sclerosis was the probable diagnosis and 16 had died of the disease, notes being obtained from the doctor or hospital records. Doubtful cases were excluded and placed among the controls. The patients were visited at their homes and the information obtained about their living conditions checked by the local doctor.

Some 65 cases were found in an area having a population of 492,049. This gave a rate of 1 per 8,600 inhabitants. They were scattered over the province along the lines of densest population. Anglesey, however, appeared to have more than its share, but not much more. Dark-complexioned types predominated (a local feature) and thin and tall persons were met with more frequently than short and stout individuals.

The distribution between urban and rural districts was about half and half, a proportion closely resembling that of the general population. In the matter of occupation, domestic and agricultural workers predominated to about the same extent in both disseminated sclerosis and the control cases. The proportion in each was about the same as that found in the general population.

The mode of life and habits were noted in the hope that some common circumstance might be detected. No instance was found of two or more cases having lived in the same house, street or district. The only recurring feature was an unsatisfactory water supply, in many cases derived from a well liable to pollution.

The results which have been recorded are therefore for the most part negative. The disease was found to be a relatively common one in North Wales, ranking in frequency however after encephalitis lethargica and its after-effects. Almost all the chief occupations were represented but the farming classes did not appear to be more likely to develop disseminated sclerosis than other diseases of the nervous system. There was no frequency among woodworkers. Evidence was also lacking to support the view that the rural incidence was greater than the urban. It is possible that had these cases been seen at a city hospital they would, coming from North Wales, have been placed in the "Country" class, whereas in reality about half of them were living in small towns.

It is open to question what importance, if any, may be attached to

the finding, in some cases, of an unsatisfactory water supply. If the disease is infective in origin and this comes through the water, surely one might expect to find instances of more than one case infected from the same supply. It should also be remembered that the inhabitants of outlying or country districts depend largely for their water supply on wells, and even in the small towns the water supply may not be up to the standard of purity of that supplied to larger towns and cities. Judging from the impressions of others, disseminated sclerosis appears to be notably frequent in remote districts such as the West of Scotland and the North of Ireland. It may be that this frequency is related more to an impure water supply than any natural features of the district or pecularity of occupations. This view is offered in no sense as a conclusion but rather as a suggestion arising out of the experience of the present work.

In conclusion the writer acknowledges with gratitude the help he has received from the medical practitioners of North Wales, who made the work possible by their ready co-operation and interest. He is indebted to the Medical Research Council for a grant to cover expenses and to Dr. E. I. Spriggs, Senior Physician at Ruthin Castle, for much valuable help and advice in the preparation of this account. He is grateful to Dr. Bradwen Hughes of the Penrhyn Hospital who enabled him to consult the case notes of the late Dr. John Owen of Liverpool, by whom many of the cases had been formerly seen. Thanks are also due to Dr. Henry Cohen of Liverpool for information relating to certain cases which had been in Liverpool.

REFERENCES.

Abrahamson, I. (1915). "A Multiple Sclerosis in Mother and Son," *Journ. Nerv. and Ment. Dis.*, **42**, 295.

Adams, D. K., Blacklock, J. W. S., Dunlop, E. M., and Scott, W. H. (1924). *Quart. Journ. Med.*, **17**, 129.

Adams, D. K. (1927). "Disseminated Sclerosis: Ætiology, Symptomatology and Occupational Incidence," *Brit. Med. Journ.*, **2**, 13.

*Alajouanine (1925). "Sur la nature infectieuse de la sclérose en plaques," *Progrès méd.*, **52**, 794.

Allen, C. E. (1927). "A Case of Familial Disseminated Sclerosis," *Lancet*, **2**, 701.

*Allen, W., and Russell, J. W. (1902). "A Case of Rheumatic Hyperpyrexia followed by Symptoms resembling those of Disseminated Sclerosis," *ibid.*, **2**, 150.

Baldwin, A. (1907). "A Case of Disseminated Sclerosis following Injury," *West London Med. Journ.*, **12**, 214.

Bailey, Pearce (1922). "Incidence of Multiple Sclerosis in U.S. Troops," *Arch. Neurol. and Psychiatr.*, **7**, 582.

Barnass (1923). Quoted by Koch (1928).

Batten, F. E. (1908). "Two Cases of a Familial Disease, the Symptoms of which closely resemble Disseminated Sclerosis," *Proc. Roy. Soc. Med.* (Sect. Neurol.), **2**, 35.

BING, R., and REESE, H. (1926). "Multiple Sklerose in der Nordwestschweiz," *Schweiz. med. Wochenschr.*, **56**, 30.

BIRLEY, J. L., and DUDGEON, L. S. (1921). "A Clinical and Experimental Contribution to the Pathogenesis of Disseminated Sclerosis," *Brain*, **44**, 150.

BLUMREICH, L., and JACOBY, M. (1897). "Zur Aetiologie der multiplen Sklerose," *Deutsch. med. Wochenschr.*, **23**, 445.

BRAMWELL, BYROM (1903). "On the Relative Frequency of Disseminated Sclerosis in this Country and in America," *Rer. Neurol. and Psychiatr.*, Edin., **1**, 12.

BULLOCH, W. E. (now GYE) (1913). "The Experimental Transmission of Disseminated Sclerosis to Rabbits," *Lancet*, **2**, 1185.

CARRIER, G. (1902). "Sclérose en plaques infantile à forme hémiplégique d'origine hérédo-syphilitique probable," *Rev. Neurol.*, **10**, 929.

CATOLA, G. (1906). "Sclérose en plaques et syphilis," *Nouv. Icon. de la Salpêtr.*, **19**, 337.

CESTAN, R., and GUILLAIN, G. (1900). "La paraplégie spasmodique familiale et la sclérose en plaques familiales," *Rev. de Méd.*, **20**, 813.

COATES, FOSTER (1930). "A Note on Disseminated Sclerosis," *Brit. Med. Journ.*, **1**, 539.

COLLINS, J., and BAERE, E. (1914). "Disseminated Sclerosis: its Frequency compared with other Organic Disease, its Etiology, &c.," *Amer. Journ. Med. Sci.*, **148**, 495.

CRITCHLEY, M., and FERGUSON, F. (1929). "A Clinical Study of an Heredo-familial Disease resembling Disseminated Sclerosis," *Brain*, **52**, 203.

DANA, C. (1921). "Multiple Sclerosis and the Methods of Ecology," *Assoc. for Research, Nerv. and Ment. Dis., N.Y.*, Report on Multiple Sclerosis, **2**, 43.

DAVENPORT, C. B. (1921). "Multiple Sclerosis from the Standpoint of Geographic Distribution and Race," *ibid.*, **2**, 8.

DAWSON, J. W. (1916). "Histology of Disseminated Sclerosis," *Trans. Roy. Soc. Edin.*, **50**, 517.

DEVIC, A., and BERNHEIM, M. (1927). "Syphilis et sclérose en plaques," *Journ. de Méd. de Lyon*, **8**, 315.

DREYFUSS, H. (1921). "Multiple Sklerose und Beruf," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, **72**, 479.

DUFOUR, H. (1916). "Méfaits de l'hérédo-syphilis tardive sur le système nerveux: sclérose en plaques—présentation d'une malade," *Bull. et Mém. Soc. méd. des Hôp. de Paris*, **40**, 715.

EICHHORST, H. (1896). "Ueber infantile und hereditaire multiple Sklerose," *Virchow's Arch. f. path. Anat.*, **10**, 173.

Idem. (1913). "Multiple Sklerose und spastische Spinalparalyse," *Med. Klin.*, **9**, 1617.

*FOXWELL, A. (1886). "A Case of Rheumatic Hyperpyrexia, with Nervous Sequlæ simulating Multiple Sclerosis," *Lancet*, **1**, 1012.

GIRONÉS, L. (1928). "Sobre la clinica de la esclerosis multiple," *Rev. méd. de Barcelona*, **9**, 581.

GOWERS, W. R. (1888). "Manual of Diseases of the Nervous System," 507.

GROSSMANN, E. (1905). "Unfall und multiple Sklerose," *Deutsch. med. Wochenschr.*, **31**, 1633.

HELPERT (1929). "Disseminated Sclerosis and CO Intoxication," *Arch. f. Psychiatr.*, **89**, 117.

HOFFMANN. Quoted by JELLIFFE, SMITH E. (1904).

JELLIFFE, SMITH E. (1904). "Multiple Sclerosis, its Occurrence and Etiology," *Journ. Nerv. and Ment. Dis.*, **31**, 446.

*JOFFROY, A. (1870). "Note sur un cas de sclérose en plaques disséminées," *Gaz. méd. de Paris*, 308.

JORDAN, B. F. (1892). "Sudden and Depressing Emotion as a Cause of Cerebro-spinal Sclerosis in a Young Woman aged Twenty-two," *Bost. Med. Rev.*, **31**, 208.

JOSEPHY, H. (1919). "Ueber multiple Sklerose bei Soldaten," *Deutsch. Zeitschr. f. Nervenheilk.*, **64**, 243.

KLAUSNER, I. (1901). "Ein Beitrag zur Aetiologie der multiplen Sklerose," *Arch. f. Psychiatr.*, **34**, 841.

KOCH, E. (1929). "Multiple Sklerose und Beruf," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, **121**, 71.

KRAFFT-EBING, R. (1895). "Zur Aetiologie der multiplen Sklerose," *Wien. klin. Wochenschr.*, **8**, 895.

LEUBA. Quoted by JELLIFFE, SMITH E. (1904).

MARIE, P. (1895). Lectures on Diseases of the Spinal Cord. London: New Sydenham Society. Lecture 12.

MCALPINE, D. (1927). "An Address on Disseminated Sclerosis, with Special Reference to its Infective Origin," *Brit. Med. Journ.*, **1**, 269.

MCGURN, W. J. (1917). "Multiple Sclerosis due to Repeated Inhalation of CO in Furnace Gas," *Medical Record*, **91**, 149.

MIURA, K. (1911). *Deutsch. Zeitschr. f. Nervenheilk.*, **41**, 146.

MONRAD-KROHN (1924). *Rev. Neurol.*, Paris, **31**, 707.

MORAWITZ, P. (1904). "Zur Kenntnis der multiplen Sklerose," *Deutsch. Arch. f. klin. Med.*, **82**, 151.

MOXON (1873). "A Case of Insular Sclerosis of the Brain and Spinal Cord," *Lancet*, **1**, 236.

MÜLLER (1905). Quoted by STEINER, G. (1922).

OPPENHEIM (1896). "Zur Lehre von der multiplen Sklerose," *Berl. klin. Wochenschr.*, **33**, 184.

PALMER (1907). "A Case of Disseminated Sclerosis following Injury," *West Lond. Med. Journ.*, **12**, 219.

PEMBERTON, R. (1903). "A Case with some of the Symptoms of Multiple Sclerosis due to Trauma," *Journ. Nerv. and Ment. Dis.*, **32**, 655.

*PERDRAU, J. R. (1928). "The Histology of Post-vaccinal Encephalitis," *Journ. Path. and Bact.*, **31**, 17.

*PERDRAU, J. R., and PUGH, L. P. (1930). "The Pathology of Disseminated Encephalomyelitis of the Dog," *ibid.*, **33**, 79.

*PETTE, H. (1928). "Ueber die Pathogenese der multiplen Sklerose," *Deutsch. Zeitschr. f. Nervenheilk.*, **105**, 76.

PREISSNER, F. (1928). "Isolierte Dauerschadigung des Ruckenmarks durch Blitzschlag ähnlich dem Bilde der multiplen Sklerose," *Deutsch. med. Wochenschr.*, **54**, 1164.

REYNOLDS, E. S. (1904). "Some Cases of Familial Disseminated Sclerosis," *Brain*, **27**, 163.

ROBINSON, G. W., and ROBINSON, G. W., JUN. (1929). "Eight Cases of Multiple Sclerosis in Three Generations of One Family," *Journ. Amer. Med. Assoc.*, **92**, 892.

*SPILLER, W. G. (1900). "A Case of Malaria presenting the Symptoms of Disseminated Sclerosis, with Necropsy," *Journ. Nerv. and Ment. Dis.*, **27**, 643.

SPILLER, W. G., and CAMP, C. D. (1907). "The Clinical Resemblance of Cerebro-spinal Syphilis to Disseminated Sclerosis," *ibid.*, **34**, 660.

SPILLER, W. G., and WOODS, A. H. (1909). "The Syphilitic Form of Multiple Sclerosis," *ibid.*, **36**, 372.

SPRAWSON, C. A. (1927). "Disseminated Sclerosis amongst Indians in India," *Trans. 7th Congr. Far East Assoc. Trop. Med.*, **1**, 8.

STEINER, G. (1922). "Multiple Sklerose," *Ergebn. d. inn. Med. u. Kinderheilk.*, **21**, 274.

STEWART, G. (1927). Oxford Medicine: "Disseminated Sclerosis."

STRUMPELL (1896). "Zur Pathologie der multiplen Sklerose," *Neurol. Zentralbl.*, **21**, 961.

*TORTI and ANGELINI (1893). "Infezione malarica cronica coi sintoni della sclerosi a placche." Abstract in *Neurol. Zentralbl.*, 858.

WECHSLER, I. S. (1921). "Statistics of Multiple Sclerosis," *Assoc. for Research Nerv. and Ment. Dis., N.Y.*, Report on Multiple Sclerosis, **2**, 26.

WILLIAMSON, R. T. (1903). "On the Etiology and Pathogenesis of Disseminated Sclerosis," *Med. Chron.*, **37**, 261.

WILSON, I. G. H. (1927). "Disseminated Sclerosis: the Rat as a Possible Carrier of Infection," *Brit. Med. Journ.*, **2**, 1220.

* Consulted but not quoted in text.

CENTRAL MECHANISM OF THE REFLEX ARC.

A Description of a Ballistic Model in Terms of which to Unify Explanations of Spinal Reflex Activity and Certain Changes in the Voluntary Electromyogram in Man.

BY E. A. BLAKE PRITCHARD,

Assistant in the Medical Unit.

(From the Neurological Department, University College Hospital.)

In a recent paper (*Brain*, 1930, liii, 344) it was shown that the changes which take place in the voluntary electromyogram as a result of fatigue could be explained in terms of a mechanism having certain specified properties somewhere on the motor side of the reflex arc central to the lower motor neurones. Since this mechanism must participate in all the activities of this reflex arc which lead to a motor discharge, it must be determined how far the properties here ascribed to it would influence its behaviour in local reflex activity.

In 1925 Sherrington (*Proc. Roy. Soc. Lond.*, B. 1926, xcvii, 519) put forward a scheme of reflex excitation and inhibition based upon the activities of a functional unit in just this situation.

Sherrington points out that the current conception of the neuronic mechanism underlying the conduction of the nervous impulse contains certain elements which may be shared by the interneuronic mechanism responsible for its intercellular transmission. "In the Nernst theory developed by Lapicque, Hill, and others, the rise in concentration of ions for effective excitation must be in amount and rate above a certain critical value. And the theory takes account of a process inherent in the conditions attending the establishment of the local ion-concentration, which tends to take those ions out of the sphere of action, a process for which diffusion and adsorption have been assigned as probable causes. This process, when the production of further excitation-ions ceases, removes the local concentration, the excitation ceasing" (p. 520).

This conception of the production locally of some substance (ions) whose presence determines nerve-fibre excitation and conduction has been extended by Sherrington to explain the transmission of central

excitation. For this, the existence of a mechanism providing an "exciting state or agent, E," is postulated. In the same way an "inhibitory state or agent, I," is provided to mediate the transmission of central inhibition. The properties of this mechanism are defined by the following characteristics of E and I.

With regard to E, "The notion meant to be conveyed is not that of a continuous level of intensity of E, persisting, e.g., at C, after a single-shock stimulus or during a tetanic one. It is that in response to a single centripetal impulse there results, to use a term already suggested, a 'charge' of E, which shoots up to a certain amount (intensity) and then, less rapidly, declines" (p. 522). "The production of E, though a discontinuous process, can by repetition, especially of frequent and of strong centripetal impulses, lead to a continuous supraliminal residuum of E, above which runs a fluctuating intensity with fluctuations corresponding in rate of frequence with the frequence of the external stimulus" (p. 523). C is the "central organ" or mechanism above referred to, and it "must of course lie down-stream from the afferent terminals themselves" (p. 524), in "a structure which is something other than a nerve fibre" (p. 521). In the central field "extending between the terminals of the fibres of the afferent nerve and the emergent motor axon toward which they conduct, there are probably various other such loci, some at successive levels" (p. 524).

With regard to I: It stands for "a state or agent which produces lessening or total disappearance of E" (p. 528). "The Nernst theory of excitation, and the development of it by Lapicque, Hill, and others, recognize the existence of a process counter to the local accumulating of excitatory ion-concentration" (p. 528), and the effect of I "may be essentially an active acceleration of the spontaneous dissipation of an exciting agent or state, e.g., an acceleration and augmentation of that deconcentration process already taken account of in the Nernst theory of excitation" (p. 529). But I "not only accelerates the disappearance of a state of excitation, it also carries the condition of the excitable structure to a state farther removed from excitation than is its normal resting one" (p. 529). "The state or agent immediately responsible for the central inhibition does not draw its source directly from a co-existent state of excitation. It does not arise from something furnished by the state of excitation or by the exciting agent" (p. 530). But though "it is assumed that the I state or agent can be produced independently of E, just as it is universally accepted that excitation can arise and exist independently of I, that

assumption regarding I does not indicate that excitation has no relation to or consequences for the production of I, and *vice versâ*" (p. 531). It is implied with regard to I "that like E its quantity or concentration after cessation of the stimulus of the inhibitory afferent, automatically subsides or deconcentrates, and that its amount or concentration and its persistence exhibit various degrees, one factor in them being production or presence of E, which tends to neutralize it" (p. 531).

Although this centre is assumed to act by the production of two different, mutually antagonistic substances, E and I, units of which are liberated by an exciting and an inhibitory impulse respectively, the time relations of production and disappearance of each are closely alike. Observations of Beritoff and Adrian are quoted (p. 531) in support of the probability of their being, unit for unit, contrasting equivalents. This seems to be true not only of the interaction of minimal units of either, but, further, with stronger stimuli "the central inhibition-state, like the central excitatory, lasts longer, its persistence being evidenced by after-action analogous with the 'after-discharge' from persistence of E" (p. 532). Since with quiescence of the arc neither of these agents is present, the production of E and of I resembles the shifting of some central balance in directly opposed senses. "The condition of the material of the common locus seems altered in two diametrically opposite ways by the two antagonistic arcs" (p. 533).

To summarize the characteristic particulars of the system which Sherrington has postulated, we find that in the first place it lies up-stream or central to the lower motor neurone, i.e., in the position which the mechanism assumed to exist, from a consideration of the effort syndrome, must occupy.

It is normally in a condition of stable equilibrium corresponding to quiescence of the reflex arc. From this condition it is capable of being disturbed in two diametrically opposed directions—one corresponding to excitation and the other to inhibition. When so disturbed it tends of itself to return to the pre-existing condition of neutrality or equilibrium. A single exciting impulse tends to displace it to a certain degree in one direction—a single inhibitory impulse tends to displace it an exactly equal degree in the other direction. Stronger exciting influences, i.e., more exciting impulses, and stronger inhibitory influences, i.e., more inhibitory impulses, will tend to displace it to a corresponding greater degree in these two respective directions.

This tendency toward displacement is not a continuous one maintained in any way by the impulses responsible. The effect of each impulse is

rather that of "impact" than of a continuous force, resulting in a disturbance which "shoots up to a certain amount (intensity) and then, less rapidly, declines" (p. 522).

Taken together these characteristics are strikingly similar in all respects to those of the elasticity of a simple ballistic system.

But one qualification is necessary if the parallel is to be an accurate one, and here the time relations are all important. An inertialess elastic system disturbed by impact, however small, from its position of equilibrium would shoot off to infinity at once. The addition of some property akin to lag or inertia, some quality like mass, imposes a limit to the resulting disturbance and makes it proportionate to the impact. It determines the time relations both of the disturbance and of the recovery phase. Further, it provides that overshooting of the position of equilibrium which is the basis of the oscillations and which in the system under consideration here is shown as "rebound." The fact that not only is the degree of disturbance the same for antagonistically equivalent units of excitation and inhibition, but that the time relations of the disturbances also are identical, provides a very strong inducement for regarding them as oppositely directed processes acting upon a single mechanism, and for regarding the mechanism held to be responsible for the effort syndrome as capable of accounting for these other properties of the reflex arc.

Let it be assumed that immediately central to the final common path there exists a mechanism through which, and through which alone, the neurones constituting that final common path may be excited. These neurones themselves are capable only of being either excited or not excited; the central mechanism is capable of a further condition referred to as being inhibited. The mechanism has properties akin to damped elasticity and to mass or inertia. It may have other properties in addition, but these two are necessary and may prove sufficient. Excitation entails the disturbance of the equilibrium maintained under the elastic process within the system. One unit of excitation acts upon this system as an impact displacing it from its position of equilibrium in one direction. Two units of excitation will act as an impact of double the size, and so on. Units of inhibition act as impacts upon the system of exactly the same size but in the reverse direction. These impacts may be delivered in whatever condition of rest or disturbance the system may be. The system is symmetrical about its position of equilibrium so that it will be displaced to an equal amount in the two opposite directions by an equal number of excitation and inhibition

units respectively. The factor which determines excitation of the final common path or motor neurones is the degree of displacement—the greater the degree of displacement the greater the number of neurones excited—the rate of displacement having no effect upon their excitation.

Let us now take the experimental facts which Sherrington has already brought under examination, considering first those in respect of excitation alone.

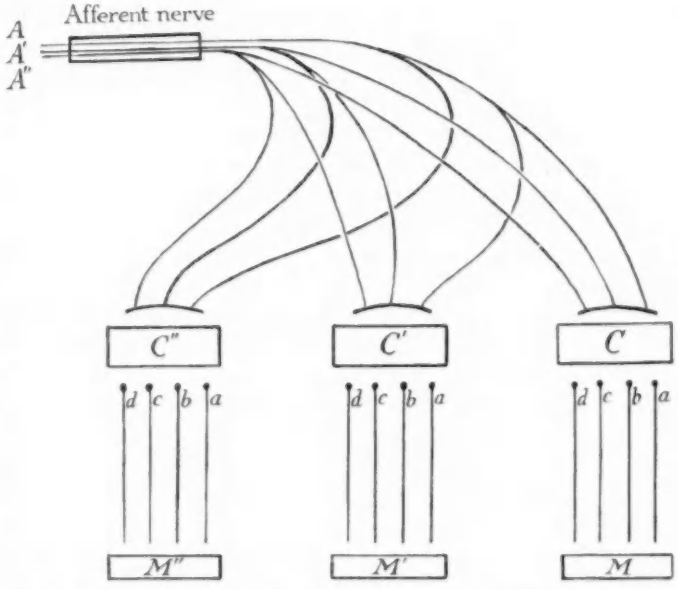

FIG. 1.—Let A A' A'' represent fibres of a purely excitatory afferent nerve. Let each of these fibres be connected with all of the central organs, C C' C''. Let stimulation of A A' A'' produce changes in C C' C'' which result in excitation of one or more of the motor neurones M *a b c d*, M' *a b c d*, M'' *a b c d*, leading to contraction of corresponding elements in the muscle units M M' M''

(1) "With increase, within limits, of strength of a single-shock stimulus applied to the afferent nerve there occurs increase of the muscular response" (p. 525).

A stimulus of small strength will excite few nerve-fibres and provide few excitatory impacts; the system will be disturbed by a certain amount. A stimulus of greater strength will provide more excitatory impacts and disturb the system by a greater amount. But if X impacts displace the system through a distance or to an amount D, 2X impacts

will displace it less than 2D, because as the displacement increases the force tending to restore the system to its position of equilibrium also increases. There will therefore be a limit to the effective increase in

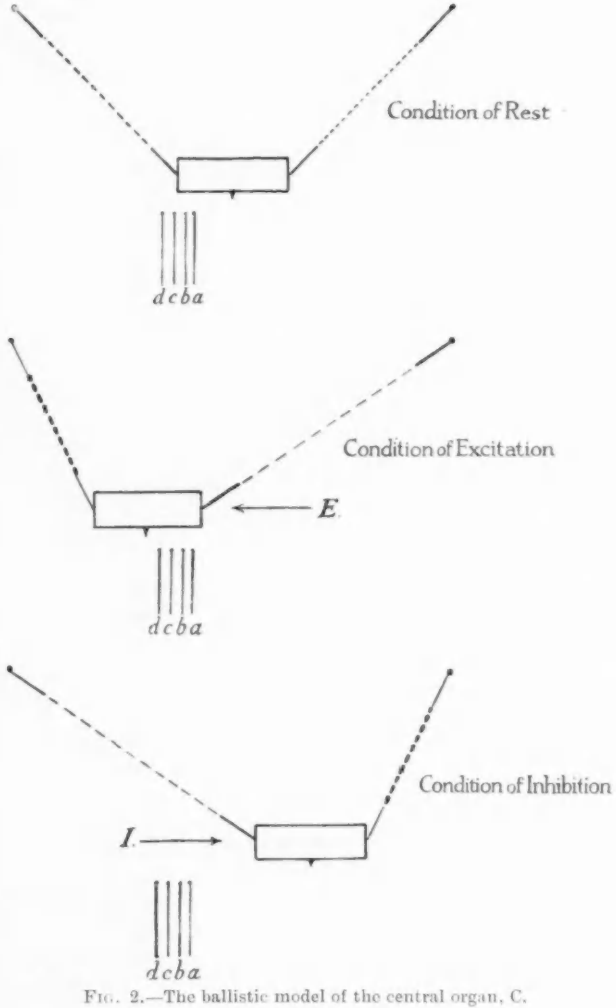

FIG. 2.—The ballistic model of the central organ, C.

displacement, and therefore to the number of motor neurones excited with increase of the stimulus, quite apart from any consideration as to the number of neurones available for excitation. Hence, not only will

there be grading of the efferent discharge and of the consequent motor response in accordance with grading of the single shock stimulus of the afferent nerve, but this grading will not be strictly proportionate, the increase in response will fall off progressively more and more rapidly as the stimulus strength is increased, and will sooner or later reach a limit beyond which no further increase will follow from increasing the stimulus.

(2) "The single-shock reflex exhibits after-discharge. With increase, within limits, of the strength of a single-shock stimulus of the afferent nerve, the reflex after-discharge is increased and prolonged."

A single stimulus providing along different afferent fibres one or more excitation units of impact will displace the system to a proportional degree in the direction of excitation. The inertia of the system provides a lag in the return to equilibrium which determines that the displacement shall outlast the stimulus for a period which will depend upon the relation between the inertia and the restoring force or elasticity. With increase of the stimulus there will be increase of the number of excitation impacts, increase in the amount of displacement and increase in the after-duration of sufficient displacement necessary to determine continuation of the motor discharge. Since there will be not only an increase in the duration of sufficient displacement to excite the motor units of low threshold, but also, the displacement being greater in the case of the stronger stimulus, an increase in the number of motor units affected, the after-discharge will be both prolonged and increased. However, just as the process discussed under (1) reaches a limit, so here also the same factors determine the limit to which this proportionate increase can be pushed by increase of the stimulus strength.

(3) "In many excitatory reflexes mere prolongation of the otherwise unaltered stimulation of the afferent nerve increases the reflex contraction" (p. 526).

After the delivery of a single excitation stimulus the system returns towards its position of neutrality or equilibrium. The degree of restoration attained at any given moment after the displacing impact is a function of the time interval. A second impact delivered before complete restoration of equilibrium will reach the system in a phase of partial recovery or partial displacement and, acting from this point, will produce a greater degree of excitation displacement than it would have done had it acted upon the system in the position of equilibrium. The smaller the interval between the delivery of the two stimuli the smaller will be the amount of recovery achieved, i.e., the greater will be the

actual displacement when the second arrives, and the greater will be the final amount of displacement provided by both stimuli in succession. Prolongation of the otherwise unaltered stimulation of the afferent nerves, by providing a succession of afferent impulses and a succession of excitation impacts, will thus cause a gradually increasing degree of displacement which will increase the number of motor neurones affected and hence also the reflex contraction. This process has been given the name "recruitment" by Sherrington.

It will be noticed that since the restoring force increases with the amount of displacement, with a given stimulus (i.e., with a given number of simultaneous excitation impacts per stimulus), a degree of disturbance will sooner or later be reached at which, under the increased restoring force, the amount of recovery which has taken place after each stimulus will become equal to the amount of disturbance which the subsequent stimulus is capable of providing at that degree of displacement. After this point is reached further prolongation of the stimulus will produce no further maximal displacement, so that "the recruitment obtainable by prolonging a given stimulus of the afferent nerve does not, if that stimulus be below a certain intensity, proceed so far as to enlist all the motor-units of the whole motor-unit aggregate, however long the duration may be extended" (p. 526).

This successive summation of effects will clearly account also for the fact that "mere prolongation, e.g., by repetition, of a brief external stimulus of the afferent nerve has usually the effect that a stimulus, which when brief is subliminal, becomes by prolongation, e.g., repetition, liminal or supraliminal" (p. 521). Sherrington has shown that this result is explicable upon the basis of some central structure which "has, unlike nerve-fibre, no absolute refractory phase, and has, as have many other cell-structures, including skeletal muscle-fibre itself, a property of summating its successive reactions when these are not too far apart in time" (p. 521). Again, with a slow rate of repetition the inter-stimulus recovery will be greater in amount than with a high frequency of repetition. Therefore, rapidity of stimulation will provide not only a greater mean value of continued displacement but also smaller degrees of variation in this displacement, so that "the individual fluctuations will be smaller, and the mean intensity higher, in proportion, other conditions equal, as the frequence of the stimulus is rapid" (p. 523).

(4) "'After-discharge' contraction will exhibit no rhythm corresponding, as does that of the stimulation contraction period, with that of the external stimulus" (p. 523).

From the considerations detailed in (3) it is clear that the fluctuations in the motor discharge during a series of stimuli in slow succession to an excitatory afferent nerve will be in step with the stimuli themselves—the rhythm of stimulation and the rhythm of discharge will be identical. When the series is interrupted there will be some after-discharge (see (2)), but this after-discharge will be subject to no fluctuations and will therefore exhibit no rhythm corresponding, as does that of the stimulation contraction-period, with that of the external stimulus.

(5) "Increase of strength (within limits) of the stimulus applied to the afferent nerve shortens the initial latent interval of the reflex" (p. 526).

Increase of the strength of the stimulus provides an increase in the number of simultaneous excitation-impacts, an increase in the rate at which the inertia of the system is overcome and a decrease in the time necessary for the attainment of any particular degree of displacement. This will entail a shortening of the initial latent interval of the reflex.

(6) "Increase, within limits, of strength of stimulation of the afferent nerve increases the muscular response, not only when the stimulus is a single shock, but also when it is tetanic" (p. 527).

Clearly the change from increase of a single shock stimulus to increase of strength of a tetanic series provides an increase not only of the number of simultaneous excitation impacts derived from a single stimulus but also an increase in the number of the simultaneous impacts occurring at each repetition of the stimulus when this is tetanic. Therefore increase of the strength of tetanic stimulation will, by increasing the amount of additional displacement per stimulus, increase also the mean value of the maintained displacement and hence the average number of motor neurones involved and through them the muscular response. This increase will be subject to the same limiting factors as have been discussed under (1).

(7) "Persistence of after-discharge, both under single-shock and tetanic stimuli, attaches in one and the same reflex-sample very unequally to different individuals of the 'motor-unit' group engaged" (p. 527).

The delay in the recovery process, which is the result of the inertia of the system, determines the after-discharge. Since recovery is progressive those motor neurones which require for their excitation greater amounts of displacement will be provided with this necessary condition for a shorter period following the cessation of any given stimulation than will the motor neurones which require smaller amounts

of displacement. Further, with variations in the strength and effective value (repetition-rate, prepotency, &c.) of the stimulus persistent high degrees of displacement will be less frequently met with than will persistent low degrees of displacement, so that the former motor neurones will be affected not only to a less degree in each case, but also less often in all cases than will the latter.

These facts and explanations are concerned with disturbance of the system in one direction only, i.e., that of excitation. It must now be considered how far the same properties will provide an explanation for the effects of inhibiting stimulation.

(8) "Increase, within limits, of the strength of the stimulus of the inhibitory afferent increases the amount of relaxation which the inhibitory reflex can produce in the contraction of a given excitatory reflex" (p. 534).

Increase of the strength of the stimulus provides a greater number of inhibitory impacts and will tend to produce a greater amount of displacement in the direction of inhibition. This, summing algebraically with the pre-existing excitatory displacement, will diminish this excitatory displacement to a greater degree, produce an increase in the number of motor neurones released from activation, and increase the amount of relaxation in the muscle response.

As the strength of the stimulus producing inhibition is progressively increased a stage will be reached at which the excitatory displacement is reduced wholly to zero, when total relaxation will occur and there will remain no after-discharge. With further increase in the strength of the stimulus the reduction in the excitatory displacement increases still further, so that this becomes negative in amount, i.e., residual inhibitory displacement is left which is gradually reduced to zero by the elastic restoring forces of the system. The delay in this restoration of equilibrium provides the "inhibitory after-action." This explains why it is that against a given excitatory reflex "the weak stimulus of the pure inhibitory afferent produces a lesser immediate 'partial' relaxation of contraction and less curtailment of after-discharge contraction than does the moderate stimulus, while the strong stimulus causes immediate 'total' relaxation, precludes after-discharge contraction altogether, and leaves in regard to some of the motor neurones an inhibitory after-action" (p. 535).

(9) "The central action evoked by the same stimulus of the inhibitory afferent which causes only small relaxation of the contraction excited by a strong stimulus of the excitatory afferent can cause large relaxation

of the contraction excited by a weak stimulus of the excitatory afferent" (p. 536).

A given stimulus of an inhibitory afferent provides a certain number of inhibition impacts. The effect of these summates algebraically with a large excitation displacement in the case of the strong stimulus to the excitatory afferent and with a small excitation displacement in the case of the weak stimulus. In the former case the displacement will be reduced to a smaller degree, the number of motor neurones thrown out of activation will be diminished and the relaxation will be less.

(10) "Experiment shows that, within limits, mere prolongation or repetition of the otherwise unaltered stimulus applied to the inhibitory afferent increases the amount of inhibitory relaxation of a given reflex contraction" (p. 536).

It is unnecessary to elaborate in appropriate detail the way in which this result can be as readily explained. This inhibitory recruitment can be explained on a basis exactly similar to that outlined in explaining excitatory recruitment (§ 3).

(11) "Within limits, increase of strength of the inhibitory afferent's stimulus gives increase of the amount of relaxation of a sampled excitatory reflex" (p. 537).

Clearly the increase in relaxation effect shown to be explicable for single inhibitory-afferent stimuli may be also shown to be explicable for tetanic stimuli—just as the excitation response was shown to increase with increase of both single-shock and tetanic stimuli to an excitatory afferent.

(12) "An intercurrent stimulation of the inhibitory afferent applied in the course of an excitatory reflex can, besides producing relaxation partial or complete of the reflex contraction, be followed after withdrawal of the inhibitory stimulus by temporary impairment of the restoration of the contraction under continued unaltered application of the excitatory stimulus, the returning contraction exhibiting slower development than did the corresponding part of the original contraction at initiation of the excitatory reflex before occurrence of the inhibition. Also the impairment of return after a given inhibitory stimulus is greater as against a weaker excitatory stimulus than as against a stronger" (p. 537).

Each stimulus to an inhibitory afferent nerve provides a certain number of inhibition impacts which diminish the excitation displacement by a proportionate amount. With continuation of the excitatory stimulation the full pre-existent excitation displacement is restored.

But immediately following the delivery of the inhibition impacts the system will be moving towards the position of equilibrium. Therefore before the excitation displacement can be restored the whole system must be retarded in its equilibrium-recovery phase, arrested and set again into motion in the direction of excitation. By virtue of its inherent inertia these processes will require a definite time for their occurrence in sequence ; also a given number of excitation impacts will produce less further shift in the direction of excitation when the system has momentum in the reverse direction than when the system has none. For these reasons the time taken to increase the excitation displacement from the amount present at the cessation of inhibition to the full amount present before inhibition, will be greater than that originally occupied by the same amount of increase at the initiation of the excitatory reflex before the occurrence of inhibition. Also since momentum in the direction of inhibition is constant for a given inhibitory stimulus, it will delay excitation recovery to a greater extent when the excitation impacts are few than when they are many, i.e., the impairment of return will be greater when the excitation stimuli are weaker than when they are stronger.

(13) " A stimulus of the inhibitory afferent counteracts the effect of the stimulus of the excitatory afferent more in regard to the motor-units of higher threshold for the excitatory afferent than in regard to those of lower threshold for that afferent, and does so both in respect to the stimulation period of the excitatory afferent and to the after-discharge period " (p. 538).

A given inhibitory stimulus will only affect a proportionate amount of shift in the direction of inhibition, i.e., only diminish the excitation displacement by a certain amount. The motor neurones which require for their activation greater amounts of excitation displacement will not only find this reduced below threshold value as a result of various inhibitory stimuli more frequently, but they will be deprived of the requisite amount of excitation displacement earlier, and have it restored later, than those which require smaller amounts of displacement. Moreover, the inhibitory impacts, which accelerate the equilibrium restoration tendency having play after cessation of excitatory stimulation will, by hastening this restoration, diminish the after-discharge. Since also the greater degree of excitation displacement necessary to activate the motor neurones of higher threshold will be less rarely left over, and certainly left over for a shorter period, than that required for the motor neurones of lower threshold, the former will suffer greater eclipse from

inhibition than will the latter, in respect also of the after-discharge period.

(14) "With a given excitatory reflex a stimulus of the inhibitory afferent can more readily relax the after-discharge contraction than cause relaxation of the contraction during the actual course of the excitatory nerve-stimulation" (p. 538).

Since during the after-discharge period the system is already moving in the direction of excitation displacement reduction, i.e., of inhibition displacement increase, a stimulus of the inhibitory afferent will produce more rapid and more extensive change in the direction of inhibition than it will when its inhibition impacts impinge upon the system during maintained excitation displacement. Therefore it follows that it will more readily affect the after-discharge contraction than the contraction during the course of excitatory nerve stimulation.

(15) "The later in the course of the after-discharge the inhibitory stimulus be applied the less strong need that stimulus be in order to cause relaxation of the after-contraction" (p. 538).

The later in the course of after-discharge the inhibitory stimulus is applied the greater will be the velocity of the system in the direction of inhibition and the fewer the number of inhibition impacts (the less the strength of the stimulus) required to diminish the existing excitation displacement by an amount which will reduce it below the value required by the motor neurones for their activation.

(16) "The after-discharge contraction does not tend to return after an intercurrent inhibition has interrupted it" (p. 538).

Since the system is already travelling in the direction of inhibition when the inhibitory impacts arrive, in the absence either of further excitatory stimuli or of inhibition rebound due to the momentum of the system on its return from any very considerable inhibition displacement (if this results), there can be no tendency for any further movement in the direction of excitation, i.e., no further tendency for the return of after-discharge.

(17) "The latency of the reflex inhibition is less with stronger stimuli, single-shock or tetanic, of the inhibitory afferent than with weaker, and correspondingly recruitment of inhibition proceeds more quickly under stronger tetanic stimuli of that afferent than under weaker" (p. 538).

These results are fully explicable as determined by the inertia of the system. The argument is precisely similar to that detailed in Sections (5) and (6) for the latency and recruitment of excitation effects and need not be repeated in respect of inhibition effects.

(18) "Inhibitory 'eclipse' of the after-contraction occurs, and takes place earlier, other conditions equal, the stronger the stimulus of the inhibitory afferent" (p. 539).

The stronger the stimulus to the inhibitory afferent the earlier will the excitation displacement be reduced below threshold value and the greater will be the likelihood of its total reduction upon cessation of excitatory stimulation.

Sherrington has drawn attention to the long latency with which the after-discharge-reduction effect may follow application of the inhibitory stimulus. He finds that this can be illustrated by means of his scheme and diagram if "it be supposed that owing to the circumstances, e.g., state of the central organ, the value of E be throughout greater than was actually allowed to it." We have seen that a limit beyond which increase of the excitatory stimulus leads to no further increase of the response is imposed by the increase of the elastic restoring force with increase of the displacement. Clearly another factor determining a similar limit is also present, i.e., maximum number of motor neurones which can be activated by the mechanism. It is improbable that any considerable proportion of the motor neurones require degrees of excitation displacement which approach the maximum attainable. It is much more likely, since it is a system which is characterized by changes accompanied by momentum, that it is capable of excitation-displacement to a degree which lies considerably beyond that which is required for activation of all the motor neurones innervated from it. That this is so follows also from the fact that upon cessation of a reflex contraction the after-discharge contraction commonly persists at the same level as the concurrent excitation contraction, and only later falls gradually away. This would follow if the level of displacement maintained by the constant excitatory stimulation is considerably greater than that required by the threshold of the motor units activated. Although the recovery begins immediately the excitatory stimulus ceases, there will be the more delay before the displacement has been reduced to the above threshold level, the higher the maintained excitation displacement level, and throughout the period of this delay the after-discharge contraction will be unaffected.

Further, an inhibitory stimulus applied during the course of excitatory stimulation may not suffice to reduce the existing excitation displacement below the threshold value of any of its activated neurones. Yet it certainly will effect some reduction: a reduction which will show itself by diminution of the after-discharge. The smaller amount of

displacement will, after cessation of the excitatory stimulation, take less time for further reduction to below threshold level than would have been required for the original amounts of displacement prior to the delivery of the inhibitory stimulus. "Therefore the after-discharge contraction, although it may still be a long-persisting one, will yet not be so prolonged as when no intercurrent inhibitory stimulus is given, although that stimulus as judged by absence of immediate outward (relaxatory) result be a seemingly ineffective one" (p. 539).

We have seen previously, Sections (5) and (6), that the increase of the restoring force with increase of displacement makes it more difficult for a given number of excitation impacts to increase the displacement when this is already considerable than when it is small. It follows also that tetanic stimulation must be continued for a long period to restore a given amount of excitation displacement, when the original level of this is high, than when it is low. Therefore a slight inhibitory stimulus which may achieve a considerable reduction of excitation displacement from a high level (Section 12) may in this way very much delay the return to the original level of displacement which follows its cessation, and considerably curtail the after-discharge after a very long latency.

(19) "An inhibitory stimulus delivered during the stimulation period of the excitatory reflex may fail to cause at delivery any relaxation of the reflex contraction, and yet produce in the 'after-discharge period' an eclipse of contraction which is 'total,' i.e., affects all the motor neurones engaged in the excitatory reflex, thus showing that though seemingly effectual on none of those motor neurones at the time of its occurrence, it yet affected all of them" (p. 540).

An inhibitory stimulus whose strength is sufficiently well adjusted in relation to concurrent excitation, may reduce the amount of excitation displacement down to, but not below, the threshold level for any of the neurones involved. It will thus not produce any relaxation of the reflex contraction. There may, however, be comparatively so very little extra excitation displacement left that upon cessation of the excitatory stimulus the motor neurone activities fall off at once and the eclipse of the after-discharge is "total."

(20) "The inhibitory after-action persists longer after cessation of a stronger than after cessation of a weaker stimulus of the inhibitory afferent, other conditions equal" (p. 539).

Since the inhibition impacts supplied by the stronger inhibitory stimulus will result in a displacement of the system further in the

direction of inhibition than will result from the weaker inhibitory stimulus, the delay in recovery from inhibition will be longer in the former case. It readily follows also from this that "the latency of a post-current excitatory reflex of given strength is longer, other conditions equal, the stronger the precurrent inhibitory reflex, and the closer the stimulus of the excitatory afferent follows on cessation of the stimulus of the inhibitory afferent" (p. 539).

(21) "A precurrent stimulation of the inhibitory afferent, even, though showing no effect on the resting muscle, may prevent entirely, or retard and diminish, the contraction response of a following stimulation of the excitatory afferent" (p. 541).

In the system here defined a given inhibitory stimulus would be expected invariably to result in the same amount of change within the system. The way in which this change would influence the motor neurones which it has the power of activating would depend entirely upon the degree of displacement and the momentum of the system at the moment at which the given inhibitory impacts arrive. Similarly, a given excitatory impulse will have invariably the same effect upon the system producing momentum in the direction of excitation displacement or reducing momentum in the direction of inhibition displacement.

Thus a precurrent stimulation of an inhibitory afferent will give the system a momentum in the direction of inhibition. A following stimulation of the excitatory afferent will produce momentum in the reverse direction which may be completely used up in overcoming the inhibition momentum (in which case no displacement in the direction of excitation will occur, no motor neurones will be excited and no contraction response will follow), or which will be used up in a greater or less degree, determined by the relative values of the two momenta, and the time interval between the moments of delivery of the two stimuli. In the second case the production of displacement in the direction of excitation will be retarded and diminished in a corresponding degree, the activation of the neurones will be retarded and the number affected diminished, so that the resulting contraction response will suffer a corresponding delay and diminution.

It is clearly not essential for the production of this effect that the inhibitory stimulus should be continued up to the moment of delivery of the excitatory stimulus, so that "even in instances where the stimulation of the inhibitory afferent is withdrawn prior to the following delivery of a stimulus to the excitatory afferent, that latter stimulus if

brief (e.g., a single break-shock), of moderate strength, and quite closely ensuent after cessation of the inhibitory stimulus, will not cause contraction" (p. 541).

The strength of any stimulus, inhibitory or excitatory, has been defined here merely in terms of the number of inhibition or excitation impacts repeatedly delivered upon the system in question, and not in terms of the conditions (i.e., current strength and site) of stimulation.

A given inhibitory stimulus may impart to the system much more momentum in the direction of inhibition than is contributed in the reverse direction by an excitatory stimulus similarly delivered but to a different nerve. Such a stimulus will not only produce a much greater amount of displacement but will produce a given amount of displacement in a much shorter time. Therefore the system provides for the circumstances in which a reflex contraction is precluded from following as the result of an excitation stimulus, by a subsequently delivered inhibitory stimulus, provided that this falls in the earlier course of the latent period for the excitatory reflex.

From these considerations it appears that the postulation of a mechanism such as has been described having the properties of mass, which endows it with inertia and momentum, and of elasticity, provides a simple explanation for the observed facts of both excitation and inhibition within the reflex arc.

"Conduction along reflex arcs presents in contrast to that along nerve-trunks characters that may be figuratively described as indicating inertia and momentum" (p. 541).

The reflex-inertia is held to account for temporal summation and recruitment; the reflex-momentum for after-discharge and inhibitory after-action. But "the simple analogy cannot be taken closely, because 'reflex inertia' may be practically absent in cases where considerable 'reflex momentum' is present, and *vice versâ*" (p. 542). Since in any known mechanical system inertia and momentum are both functions of the mass, it is difficult to see how they can be expected to vary independently under purely external influences without postulating some intercurrent reversible alteration—such as in the distribution of the mass—within the system itself.

It is here suggested that if the system is regarded as having in addition to mass the property of elasticity this difficulty is overcome and these discrepancies between theory and observation disappear.

It has been shown above that a system having the properties of mass and elasticity would be expected to behave in a way calculated to

give the observed effects as a result of definite excitatory and inhibitory influences. In this scheme the mass of the system contributes the inertia which underlies the phenomena of temporal summation and stimulus—response grading, and that the elasticity provides an adequate basis for the explanation of after-discharge and inhibitory after-action. The occasional lack of parallelism between recruitment and after-discharge is sufficient to lead to hesitation in ascribing them both to manifestations of a single property. There is, however, no reason why different reflex systems having each the same properties should not vary in their possession of different amounts of each—in fact, from a consideration of the much greater facility of certain reflexes it is probable that such differences do occur.

Since we have throughout been inferring the characteristics of the system postulated from the reflex behaviour in which it plays a part, it introduces no further element of complication if we decide that those central systems which underlie reflexes which show exaggerated recruitment and minimal after-discharge have small mass and great elasticity, whereas those which mediate other reflex activities showing minimal recruitment and much after-discharge have much more mass and little elasticity.

SUMMARY.

(1) In a previous paper it was shown that certain changes in the voluntary electromyogram in fatigue and in some pathological conditions probably had their origin within the central nervous system in a specified situation.

(2) The existence of a functional unit in this situation was postulated and the properties of such a mechanism by virtue of which these changes appeared were discussed.

(3) In the present paper a mechanical model is described and its behaviour examined when it is subjected to units of equal and opposite forces.

(4) It has been shown that if by this model be represented the nervous mechanism above postulated, and by the opposing forces the impulses, excitatory and inhibitory respectively, supplied along an afferent nerve, then its behaviour is in every respect in accord with the observed facts of spinal reflex action through the arc in which the nervous mechanism must be located.

(5) From this it is inferred only that the suggested localization of the site of origin of the changes in the voluntary electromyogram is not inconsistent with the observed facts of spinal reflex activity.

CLINICAL AND ANATOMICAL STUDIES ON TWO CATS WITHOUT NEOCORTEX.

BY GEORGES SCHALTENBRAND
AND
STANLEY COBB.

(From the Department of Neuropathology, Harvard Medical School, Boston, Mass.)

CONTENTS.

	PAGE
Introduction	449
Protocol 1—Thalamus Cat, "Mary"	450
Protocol 2—Striatum Cat, "Kleopatra"	453
Summary of Protocol 2	457
Records of Activity of the Cat without Neocortex	459
Studies on Rotary Nystagmus and after Nystagmus in the Animal without Neocortex	460
Electrical Excitation of the Rest of the Brain on March 18, 1927	468
Summary of the Excitation Experiment	473
Necropsy	474
Microscopical Examination of the Brain	474
Summary of the Anatomical Findings	484
Discussion	487

Introduction.

Goltz was the first to keep a dog without forebrain alive for a long period; since then a few other investigators have succeeded in the same experiment. We mention Rothmann, senior, who operated on a dog; Dusser de Barenne, who operated on two cats; Zeliony, on dogs; Dresel and Rothmann, also on dogs; and Karplus and Kreidl, on monkeys. The general conclusion from these experiments is that higher mammals can live without cerebral cortex. They are able to stand and to walk; they have normal muscle tone; they are able to perform isolated movements of the extremities; they keep a normal body temperature, and have a normal rhythm of wakening and sleeping. They show signs of different emotional states such as satisfaction (purring in cats) and anger. They react to sounds, but they appear to be completely idiotic, if such a word may be applied to animals; they do not recognize particular sounds, and do not recognize objects by vision, though the pupillary reflexes are intact. When the rhinencephalon is intact the animals are able to find their food by smell and to eat spontaneously.

The recent clinical interest in the pathology of the basal ganglia suggests new experiments in order to find out whether there is a difference between animals where the cortex only has been removed, and others where both the cortex and the striatum have been removed. In order to contribute to this problem we developed a technique which enabled us to remove one hemisphere of the brain [18] without much danger to the life of the animal. The removal of the second hemisphere, however, proved to be a very difficult task. Out of six animals operated upon, four died within a few days after the second operation from hæmorrhage, infection or "broncho-pneumonia." One "thalamus cat" was kept alive for nine days, and one "striatum cat" survived the second operation until we killed her five months later. The present paper deals with the two animals which survived the second operation for a considerable time.

The technique of the operation differed somewhat from the usual. We worked with local anæsthesia, using a 1 per cent. novocain solution. In order to keep the animal quiet we administered bulbocapnine hydrochloride which produces a kind of "Parkinsonian state" lasting for an hour or two. It was necessary to close the carotid arteries with clamps under ether anæsthesia and to open them about half an hour after the completion of the operation. A description of this technique has been published [18].

The details of the clinical examinations can be seen from the protocols. In the striatal animal we made special examinations, including tests of ocular nystagmus, determination by graphic records of the activity of the animal, and electrical stimulation of the residual brain. These examinations will be summarized in special chapters.

Protocol 1. *Thalamus cat, "Mary."*—The *left hemisphere* was removed anterior to the thalamus on July 22, 1926. Immediately after this operation there were torsion spasms to the right side; next day these spasms began to disappear and occurred only during periods in which the general reactivity of the animal was diminished. Between the spasms the animal made circus movements to the left. There were some choreic twitches of the head. Whenever the animal started to walk after a period of rest, the right foreleg developed a tremor. The choreic movements, the torsion spasm to the right and the tremor disappeared soon, and only those symptoms remained which are typical of hemi-decortication, namely hypertonus of the crossed antigravity muscles, a slight paresis and ataxia of the crossed side, and crossed hemianopia. There were the following peculiarities: The animal made very strong circus movements to the left side. It often happened, for instance, that in attempting to eat she missed the food jar four or five times, because she

deviated to the left, and was obliged to circle round for another attempt. When the animal was blindfolded, the direction of the circus movements was reversed, the animal now circling to the right. When standing the body always inclined to the left a little. The left pupil and the left palpebral fissure remained narrower than the right.

On October 5, 1926, the *right hemisphere* was removed anterior to the thalamus. There was a definite hydrocephalus of the right ventricle. Five hours later the animal was taken from the operating table. She lay in the left recumbent position and moved the right extremities strongly, the left weakly and elevated her head.

October 6: Vomited during the night. Walks steadily, purrs when petted.

October 8: The animal makes circus movements, usually keeping to one direction for several hours. It does not eat spontaneously; it swallows with excessive movements of the jaws.

October 9: The animal made circus movements to the left (fig. 1). It

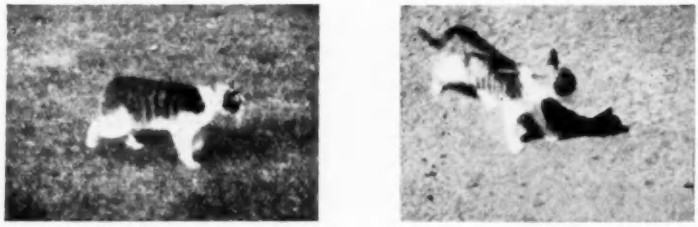

FIG. 1.

still dragged the left paws; the left extremities were hypotonic. From time to time the animal changed the direction of its circus movements without recognizable cause. The direction of the circus movements did not change on passive movement of the head. The pupils were very wide and did not react to light.

October 11: The animal was quieter, but often lay with closed eyes. Usually she circled to the right. When she was fed lying on the left side the right paws developed a clonic tremor.

October 12: The animal was becoming weaker; she stood on extended legs and had tachypnœa.

October 13: Orthopnœa and tachypnœa, the auxiliary respiratory muscles participating; eyes brilliant, no discharge from the nose. The animal looked very dry. Respiration stridorous, expiration difficult. Respiratory rate 120 a minute.

October 14: Found dead.

Necropsy.—The brain was injected with 10 per cent. formalin through the carotids and carefully dissected from the cranium. The contents of the left

cranial cavity were covered by a solid membrane of dura, connective tissue and muscle. The right side of the dural sac was filled with a jelly-like bloody exudate. Both lobi piroformes were preserved, but the left was atrophic and discoloured. Only a thin layer of tissue connected the rest of the right thalamus and the olfactory bulb (fig. 2). The left thalamus had been damaged. The brain was hardened in formalin and cut in serial sections.

The serial sections were not available when this paper was written.

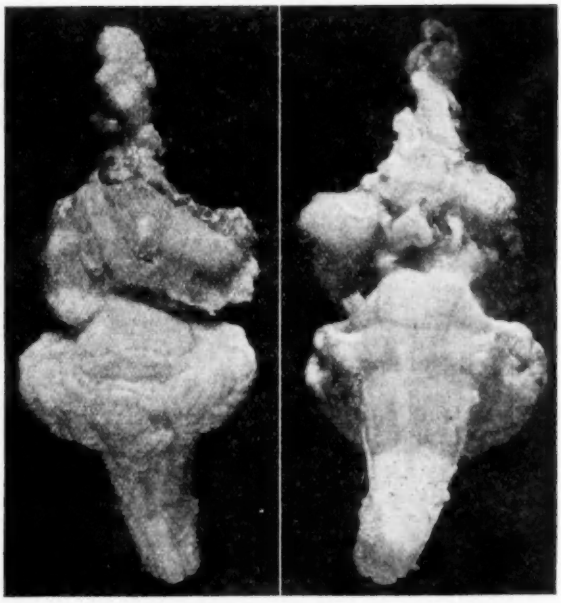

FIG. 2.

Summary.

The "thalamus cat, Mary," was observed for nine days after the second operation. Necropsy shows that the principal aim of the operation had been accomplished. The animal was able to stand and to walk but had a slight paresis of the left extremities after the second operation. States of sleep and of wakefulness could be distinguished. The behaviour of the animal was extremely dull, and it made almost constant circus movements. It changed the direction of the circus movements from time to time without apparent cause.

Protocol 2. *Striatum cat*, "*Kleopatra*."—August 4, 1926: Removal of the left neopallium. The animal received 0·06 grm. of bulbocapnine hydrochloride and developed marked catalepsy. The carotids were closed with clamps under light ether anæsthesia, and ether was discontinued. The scalp and the left temporal muscles were infiltrated with 1 per cent. novocain solution. The skull was trephined over the left hemisphere and the dura opened. The hemisphere was removed in two parts after the left lateral ventricle was opened by splitting the gyrus fornicatus its entire length. The first part included the cortex with exception of the island of Reil, the second part the island of Reil. The head of the caudate was damaged and probably also a part of the putamen was removed. There was slight hæmorrhage. Two pieces of muscle were left on the base. During the trepanation the left frontal sinus was opened; the hole was closed with wax and a flap of dura was sutured across it. The wound was closed with Michel clips and collodion dressing was applied.

After the operation the animal appeared furious. It lay in the right lateral position and could not rise. When brought into a sitting position it turned its head to the right. The right foreleg was paralysed. The animal followed the examiner with her eyes. The evening after the operation she could not stand, but always fell to the right. Periodically she had wild attacks of running movements with deviation of head and body to the right and mewing.

August 5: The animal was able to stand.

August 7: She had serous discharge from the left nostril. There was definite extensor tone of the right extremities. The animal wandered in circles to the left. The right forepaw was often tilted over. When the animal, after rest, started to walk she developed clonic spasms of both right extremities for a second or so.

August 11: The scar bulged on the left side and fluctuated; the posterior end of the wound was opened and discharged cerebrospinal fluid.

August 19: When the eyes were closed with adhesive strapping the animal tried to remove the adhesive, chiefly with the left forepaw, but sometimes also used the right; then a fine tremor of the right paw developed and its movements were clumsy compared with those of the left. There was still definite hypertonus of the extensors on the right side.

September 11: Animal was in excellent condition. The scars were healed and overgrown with hair. Pupils and palpebral fissures were equal on both sides. She wandered in circles to the left. When lying on her back, head in the symmetrical position, the right hindleg showed definitely more extensor tone than the left. The difference was less pronounced in the forelegs, but the right foreleg was more extended.

The neck-righting reflex was present to both sides, but stronger from the left than from the right. When the animal was held on a basin, head hanging down, the head was in a symmetrical position. On jumping from a chair she landed straight and kept her balance. If blindfolded she inclined to the right and backwards, falling occasionally.

She was quiet and did not move much. Occasionally her head turned to the left and she fell to the left. She tried to remove a blinder with the left forepaw, and in doing so stood on both hindlegs until she fell backwards. She turned to the left (sometimes to the right), sank down and remained there until disturbed. Finally, she fell on her left side and lay there. The shaking movements of the right extremities, which were observed during the first days after the operation, had disappeared. Weight 2·07 kg.

September 27: Until a few days ago the animal had been in excellent condition, but since the 25th it was apathetic, the scar over the left hemisphere was swollen and tender; apparently the animal had an attack of hydrocephalus, and it was decided to operate immediately.

Removal of the right neopallium.—Closure of the carotids with clamps under ether anæsthesia. Then 0·04 bulbocapnine hydrochloride was given subcutaneusly. Local anæsthesia of scalp. On opening the dura the right cortex appeared hyperæmic and fluctuated. The right ventricle was one huge cavity filled with slightly turbid fluid. The right striatum and thalamus were flat. The cortex and the remainder of the corpus callosum were removed, as well as the right choroid plexus. There was only moderate hæmorrhage; the skin was closed with clamps.

Soon after the operation the animal became restless and mewed. Half an hour later the carotid clamps were opened. In the evening all four legs had an increased extensor tone. They all moved. There was a nystagmus to the left and the head and body turned to the left.

September 28: Animal lay on its left side, was apathetic and could not stand or rise. When brought into the right recumbent position the head was raised and the body curved to the left. The animal still had some nystagmus.

September 29: Drank milk well. Could sit up if supported on the left side. The eyes occasionally showed nystagmoid movements to the left. There was definite spontaneous hippus of the pupils. The animal moved the nostrils when the head was brought over the jar of milk. Before urinating she moved around actively.

September 30: The scar fluctuated; by puncture a few cubic centimetres of bloody spinal fluid were removed.

October 1: Fluid had again accumulated and was removed by puncture. The animal walked better. She had an astonishing thirst and great hunger, never refused food and immediately started to lick and swallow as soon as the jar with food came within range of her nose. She urinated so frequently that the floor of her room was flooded.

October 2: Gait and station were unsteady. The animal sometimes fell when she shook her fur. She ate and drank hungrily, and wandered restlessly about as soon as the food was removed. The pupils reacted to light, and the eyelids were closed when a bright light was used. Sometimes the forepaws crossed by mistake and the animal tried in vain to bring them into the right position. When she started to walk the four extremities trembled exactly as the right

extremities after the first operation. The tremor gave one the impression that the animal wanted to shake off some heavy object that clung to her paws. The shaking extremity was always raised from the ground.

October 6: Weighed 2·1 kg. After dinner the animal licked her forepaws and wiped her head with the left forepaw.

October 9: The animal had diarrhœa for some days, probably because she ate too much. She was therefore given cocoa, which she disliked, instead of milk. She purred when brushed and while eating. The shaking movements of the paws had almost disappeared, but still occurred if the animal stepped into fluid; then the wet paw was shaken. The animal sat symmetrically; the body-righting-reflex-on-the-body was prompter from the right recumbent position than from the left. The animal usually walked straight forward without any tendency to circus movements. The light reflexes of pupils and of the eyelids were present. The animal opposed every attempt to turn it over on its back. The tonus of the extremities in the recumbent position was symmetrical. There were definite tonic neck-reflexes-on-the-extremities, but no tonic labyrinth reflex could be demonstrated. The neck-righting-reflex was present to both sides. The labyrinthine reflexes on the head were positive. Turning reactions of the head and of the eyes were present, also the "Sprungbereitschafts-reflex." The "lift" reactions were feeble.

October 16: The animal was very active; its gait was still unsteady, especially the hind limbs. The nose was carried near to the floor. She usually walked along the wall, and as soon as she met an object she turned around. At one corner in the fence there was a gap into which the animal often got her nose. Sometimes she spent minutes in this corner moving her nose up and down. Occasionally she jumped, and once succeeded in jumping over the fence which was about one metre high. As soon as she approached a jar filled with food she stopped and started licking movements; she often licked her paws or the floor; when she finally succeeded in reaching the food, she started to eat reflexly. When by chance the metal wall of the jar came between her teeth she bit vigorously on it. She was very particular about her food, disliked cocoa in her milk, but drank pure milk greedily. She preferred fish to other food. Sometimes she licked her forepaws, the fur of her shoulder, or even brought her hindlegs up towards her head to be licked. As a rule these cleaning movements failed, because her tongue was not brought to the desired part of the body, or was applied to some object which was met by chance, like the leg of a chair. These licking movements could always be produced reflexly by brushing the fur.

When the animal met another cat she stopped, smelled at her and might start to lick her, but no chewing or swallowing movements occurred. The animal often slept and then did not react to ordinary sounds. While awake she was extremely sensitive to sounds, the breath of the examiner was sufficient to cause a rotation of her head. As soon as the door of the fence was opened she mewed and started to run around.

October 21: The animal was demonstrated to the Boston Society of Psychiatry and Neurology.

October 25: The animal gave the impression of having some optic reactions. She was examined during the night in a long corridor, the walls of which were greyish brown, the examiner wore a white coat and the corridor was slightly illuminated by a few electric bulbs. When the examiner walked around the animal at a distance of two metres, or changed his position even at a distance of five metres, the animal followed him with her head and eyes. Every step of the examiner to the right or left was followed, and after some time the cat even walked towards the examiner and reached his shoes. As long as the examiner did not move the animal did not look towards him. There was no other evidence that the animal could recognize objects by vision. If there really were a visual reaction, it could only be a reaction to movements within the visual field. These reactions were observed several times, but were only elicited when the animal was sitting quietly. When engaged in any other occupation, as licking, eating or walking, she ignored the movements of the examiner.

When blindfolded the animal's behaviour was strange; she moved her head up and down and apparently licked the inner side of the blindfolder. At the same time she extended her forelegs more and more until she finally lost her balance and fell backwards; then she rose again and repeated the same series of movements. She could not be induced to advance a single step; finally the head sank to her side and the cat seemed to fall into a sleep. After removal of the blindfolder, she immediately started to run around.

The cat performed cleaning movements better. She spontaneously licked her sides, back and paws, but she still performed many useless licking movements in the air. On awaking from sleep she often made typical stretching movements, first stretching the forelegs and then the hindlegs in an exaggerated way.

November 15: The movements of the animal were recorded in an "activity cage."

November 28: For a few days the animal's behaviour changed completely. She was very excited and cried furiously at the slightest touch, bit into the air, scratched furiously the floor and made various sounds, as hissing and screaming, indicating anger and excitement.

December 1: A few nematodes were found in her faeces. A worm cure led to the evacuation of a lot of worms.

December 4: Animal had changed back to her old behaviour. She was again friendly, mewed instead of hissing and did not become excited when touched.

December 5 to 8: She was again placed in the registrating "activity cage."

December 9: The animal spent the greatest part of the day cleaning her fur. While engaged in this she forgot everything else; she did not stop licking when brought into a recumbent position, which usually produced intensive defence movements: she even went on licking when she was hung over a gate in a very uncomfortable position. The reaction to acoustic stimuli had diminished. Licking could be reflexly started by brushing or patting the back.

The co-ordination of the movements of mouth and tongue with the different parts of the body and the extremities had improved, but the animal still never succeeded in licking exactly the point where it had been scratched.

December 11 to 13: The animal was again examined in the registration cage, but had to be taken out on the 13th because it once more changed into a furious and excitable state. The slightest noise made the cat jump forward and attempt to bite and scratch with extended claws. Every object met on her wanderings, as the leg of a chair or empty vessel, was attacked in this way. She had developed mange on her head and her body and was given sulphur inunctions.

December 18: Mange was healed. The cat was put back in the registration cage.

December 20: The animal seemed to have a certain sense of location; for instance she sat near the bowl filled with food which was attached to the wall of the cage at the level of her head, and every time she wanted food she lifted her head, turned it to the left and brought it to the bowl. While chewing she withdrew her head, but afterwards brought it back directly to the bowl.

December 31 to January 3: Another examination in the registration cage.

January 3: The basal metabolic rate was determined when the animal had fasted for twelve hours. Weight 2·54 kg. Temperature 101·9° F. Metabolism 2·615 k. per kg. an hour.

January 6: When fasting for twenty-four hours weight was 2·54 kg., temperature 101·8° F., metabolism 2·51 k. per kg. per hour.

During February and March many experiments were made on the nystagmus of the eyes on rotation. These experiments are reported in a special chapter. On the whole the behaviour of the animal did not change, but she gradually became quieter and less active than during the first few months after the operation.

March 18: The weight of the animal was 2·9 kg. The cranial cavity was opened under bulbocapnine and local anæsthesia, and the remaining part of the brain was examined by electrical excitation. This experiment is reported in a special protocol. After this experiment the animal was killed.

Summary of Protocol 2.

The left neocortex was removed on August 4, 1926. After recovering from the first operation she developed, at the end of September, an apathetic state which was apparently due to an increasing hydrocephalus; therefore the second operation, which consisted in removing the right neocortex, was performed on September 27. The animal stood the second operation very well. A peculiar phenomenon during the first days after the operation was a clonic shaking of the extremities when the animal started to walk after a period of rest. These shaking movements had already been observed after the removal of the left

hemisphere, but then only on the right side. After a few days these shaking movements disappeared and only reappeared when the animal wet or soiled its paws.

In its best period the animal was active and moved about all day. The muscle tone and all the righting reflexes were normal; but the hind-legs were somewhat unstable and she walked with a wide base and swayed. Isolated movements of each forepaw were observed repeatedly, especially rubbing the eyes when these were closed with adhesive plaster. One of the most striking performances was cleaning the fur, and the way in which this was relearned was interesting. In the first attempts at licking the movements of the tongue and lips were excessive and accompanied by large and inappropriate movements of the head. Later, parts of the body were brought up towards the head and tongue, and finally the animal really succeeded in licking its body effectively. Until the end the animal made mistakes, and would lick the floor or the wall if it met them by chance during the cleaning procedure.

The animal ate spontaneously and found its food by smell. It showed preference for certain foods and especially for fish and milk. The hunger and the thirst of the animal were pathologically increased, especially during the first weeks after the operation. If the animal was left alone with sufficient fluid and food it would eat and drink continuously, and in consequence of this it would urinate at short intervals and get diarrhœa. The amount of fluid and food had to be therefore restricted.

The animal was very sensitive to sounds and turned the head even at the snapping of a finger-nail. It always started to move and mew when the door was opened. She did not recognize objects by vision, but exposure to light caused contraction of the pupils and blinking of the eyelids. In several experiments we had the impression that she followed with her eyes and head the examiner when he moved. This suggests that perhaps movements were perceived by vision, but of this we cannot be certain as the animal was able to hear.

Kleopatra could produce a varied scale of sounds, from the pitiful mewing which occurred every time the door was opened, to furious crying, hissing and spitting which she produced in disagreeable situations. It is of special interest that she showed different moods. In general she was gentle, but during two periods, each lasting several days, she was very excitable and reacted with definite signs of anger to every stimulus. During the first period nematodes were found in the stools and after they were eliminated the excitability disappeared. During the second period the animal suffered from mange.

The animal had a tendency to stereotyped motor performances, as eating and cleaning her fur. During these she was so much occupied that she reacted much less to external stimuli than usual.

Records of Activity of the Cat without Neocortex.

We measured the animal's activity by means of a special apparatus. The floor of one of the usual wire observation cages (about one metre in each dimension) was suspended by steel springs and the movements of one of its corners were recorded on a kymograph. The cage was placed in a separate room and was visited and cleaned only once a day. Urine was collected through a funnel. Observations were made for periods of forty-eight to seventy-two hours on seven different occasions, totalling nineteen days.

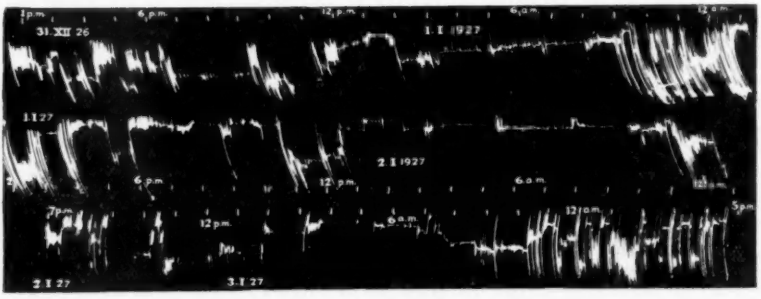

Fig. 3.

One of the records, extending over three days, is reproduced in fig. 3. These tracings show the tremendous activity of the animal, which is particularly striking when compared with that of a normal cat observed under the same conditions (fig. 4). The normal cat was relatively

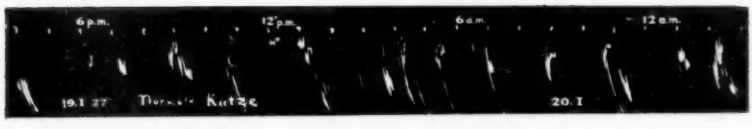

Fig. 4.

quiet; about every two hours it walked around a little, but soon settled down again. Kleopatra, however, was always on the move by day; during the night she was quieter, but still was more restless than the

normal cat. The striking difference in her behaviour during day and night cannot have been due to the daylight, as this was excluded from the room. The only changes between day and night were the noises from outside. As a matter of fact the tracings of the animal's activity corresponded to the activity of the college, which was greatest between 9 a.m. and 6 p.m., when footsteps, voices in neighbouring laboratories, the opening and closing of doors, &c., were constantly audible. We conclude that noises had a very important influence on the animal's motor activity.

On the two occasions when the animal was excitable and ill its behaviour was different. Fig. 5 shows a record of two days while it suffered from mange. The tracings by day differed little from those usually obtained, but she rarely rested by night, in fact between

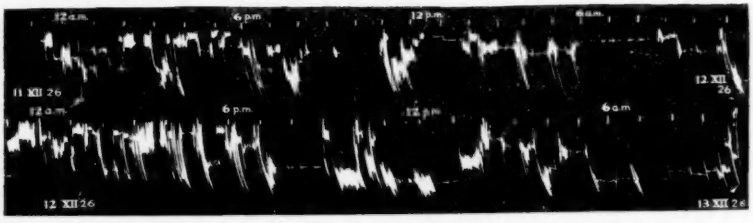

FIG. 5.

midnight and 6 a.m., when she was usually quietest, the record resembles closely a day-time tracing. This was probably due to the unpleasant stimuli excited by the mange and the gastro-intestinal parasites.

We tried to determine whether light or darkness had any influence on the animal's behaviour. The cat was usually in complete darkness while in the observation cage, but one day the room was illuminated by a 100-candle bulb. On another occasion the room was dark during the day and lit up at night. Finally, we tried to see if the animal reacted when the light was turned on and off. None of these experiments caused any significant change in the animal's behaviour.

STUDIES ON ROTATIONAL NYSTAGMUS AND AFTER-NYSTAGMUS IN THE ANIMAL WITHOUT NEOCORTEX.

Nystagmus during rotation has been studied by direct observations in man (Bárány), but its control by animal experiments has been comparatively neglected. One of the reasons for this is the technical

difficulty of observation during rotation ; another is the interference by optical influences, which can excite nystagmus by mere rotation of the visual field. Recent work by Stenvers and Holmes indicates that this optical nystagmus depends on cortical reflexes. Therefore it seemed that an animal without cortex ought to be an interesting subject for the investigation of nystagmus during rotation. There is the further advantage that in such an animal the complicated "voluntary" reactions of the cortex do not disturb the observations.

To compare nystagmus during and after rotation we built a special rotating wheel on which the cat could be fixed in any position. An arrangement of three mirrors made it possible to keep the eyes of the animal, which were illuminated by an electric lamp, under observation while the wheel was rotating. The wheel was moved by hand, and regulated by the beats of a metronome, so as to assure a fairly constant speed.

In testing the reactions of the labyrinths different factors have to be considered.

(1) The "speed of the rotation" is expressed by the "rotation quotient." This is the number of rotations per minute if the rotations were continued indefinitely.

(2) "Acceleration," which means alteration of speed during a unit of time. This comes into play at the start and at the stop of the rotation. Unfortunately we were not able to measure it, but we have assumed that both the start acceleration and the stop acceleration increase proportionally with the speed of rotation. There ought to be no acceleration between, but there can be little doubt that some of the irregularities in our observations were due to changes in the rate of rotation. Exact experiments would require that accelerations could be controlled and recorded mechanically.

One effect of the rotation is a nystagmus which starts after a short latent period ; the first few jerks are small and quick, then they become large in amplitude and equal, and finally the nystagmus gradually disappears, the individual jerks occurring at longer and longer intervals. The latency of the nystagmus can be observed especially when rotation is stopped, as then a jerk in the direction of the rotational nystagmus may be observed before nystagmus in the opposite direction develops. As the nystagmus fades out slowly, its duration in seconds is not an accurate measure of its intensity. The number of the nystagmus jerks is a better criterion. There may be, for instance, fifty jerks while a control may have fifty-one jerks, but the last jerk may come ten seconds

later and thus change the duration of the nystagmus by 20 per cent. We have, therefore, paid little attention to the duration of the nystagmus.

The following questions were studied :—

(1) What effect have different numbers of rotations at a given speed on the number of the nystagmus jerks?

(2) What effect have differences in speed, the number of rotations being constant, on the number of jerks?

We studied these two questions both in the nystagmus during rotation and in that occurring after rotation. Observations were made on rotational nystagmus at different speeds up to thirty revolutions a minute, and for as many as four revolutions. After-nystagmus was studied more extensively. The experiments were performed during February and March, 1927; the excitability of the animal during this

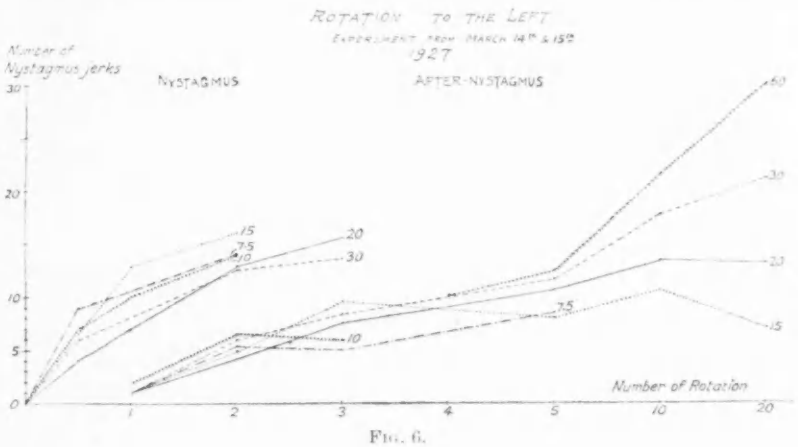

FIG. 6.

period declined considerably, and especially on March 15 to 16, perhaps owing to sores which had developed on the knees. The observations made on March 16 are not therefore included in our curves, but the figures can be found in the tables. On this date the nystagmus had a very long latency, especially the nystagmus during rotation, but the latent time of the after-nystagmus was less.

The following tables give the results of all the experiments. Each figure is usually the average of three or more measurements. The observations can be understood more easily by looking at the curves constructed from these figures. As the results of rotation to the left

and to the right were practically the same, it is sufficient to consider rotation to one side only.

Fig. 6 contains two groups of curves, the left representing rotational nystagmus, the right after-nystagmus. Every curve represents a constant speed of rotation and shows the relation between the amount of rotation and the number of nystagmus jerks for this speed. They show that definite after-nystagmus starts only after one complete revolution, while the rotational nystagmus starts immediately.

The number of after-nystagmus jerks reaches the number of rotational nystagmus jerks produced by 45° of rotation only after three complete revolutions at the same speed. During speeds of $7\frac{1}{2}$ to 60 revolutions a minute the curves are similar as long as the amount of rotation is small; but after more rapid rotation the curves of the after-nystagmus vary according to the speed. Probably the same effect could be demonstrated for the rotational nystagmus, but it was not possible to count it during more than three or four rotations. Figs. 7 and 8 show that rotational and after-nystagmus depend on the speed of rotation; each curve represents a single rotation. When the speed of rotation exceeded 30 per minute the rotational nystagmus could not be counted, but after-nystagmus was counted up to 60 rotations per minute. Rotational nystagmus was very irregular at a speed of 7·5 revolutions per minute, because slow movement could not be kept up without acceleration. At speeds of 10, 15 and 20 revolutions per minute the number of jerks depends largely on the amount of rotation; 180° of rotation produces more jerks than 90°, 360° more than 180°, and so on. The diagram shows that the number of jerks produced by a certain amount of rotation is more or less constant at various speeds.

The curves of after-nystagmus show a similar behaviour (fig. 8). At medium speeds the number of jerks depends chiefly on the amount of rotation, not on the speed. This is true, however, only as long as not more than 4 to 5 revolutions are performed. With more revolutions the nystagmus varies with the speed of rotation; the higher the speed, the more the nystagmus increases proportionally to the amount of rotation. The results of these observations are:—

(1) With small amounts of rotation (below 360°) after-nystagmus is negligible.

(2) With small amounts of rotation the number of jerks is, within certain limits, independent of the speed of rotation, but depends on the amount of rotation.

(3) Definite after-nystagmus develops only after 360° of rotation.

It is only after three or four revolutions at least that the numbers of jerks of rotational nystagmus and after-nystagmus depend essentially on the speed of rotation.

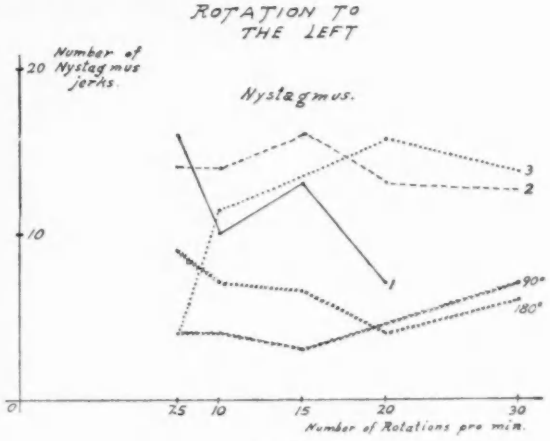

FIG. 7.

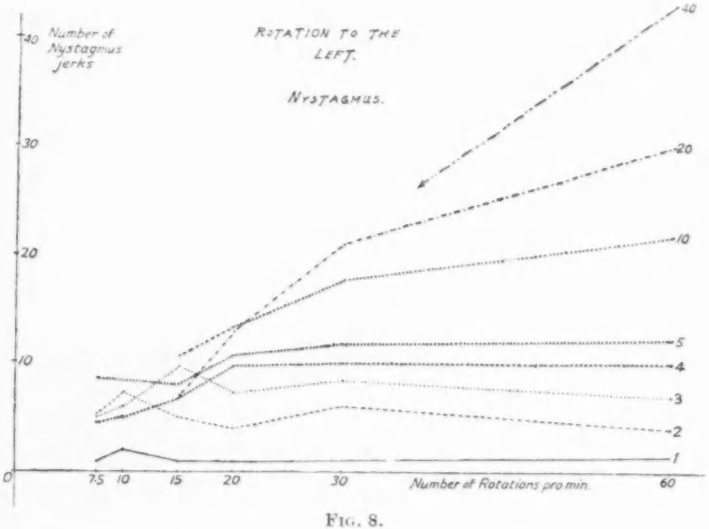

FIG. 8.

Within a certain range the nystagmus corresponds, therefore, to the amount of rotation in space; beyond this range it behaves differently. If the acceleration is too small the stimuli it excites are below the

threshold of the labyrinth. When the amount of rotation is increased, acceleration is the chief determinant of the number of jerks, and the labyrinth no longer reacts to the rotation alone. These facts are important because the amount of rotation that excites a reaction is within the range which occurs commonly during the natural movements of the animal. The reactions to acceleration, beyond this range, are reactions to non-physiological stimuli. They may be useful for the otologist, but they are a disadvantage to the animal. This statement of course holds good for rotational nystagmus only ; it is obvious that the maintenance of equilibrium needs physiological reflexes to acceleration.

These observations corroborate entirely the earlier observations of Mach [10], Breuer [3], Brown [5], Bárány [1], Masuda [13], and others on intact man and animals. They prove that the forebrain is unnecessary for all those features of rotatory nystagmus and after-nystagmus which have been described.

Our observations add nothing new to the theory of the functions of the labyrinth. They are compatible both with the older theory of Breuer [3] and Brown [5], that the labyrinthine reactions correspond to a real movement of the endolymph : and with the more recent theory of Mach [10] and Bárány [1], that the cupula of the labyrinth reacts only to acceleration, and that this reaction excites a mechanism in the nervous system which causes the nystagmus, and which can be inhibited by an impulse of the opposite direction if it appears before the mechanism has completely discharged.

The fact that rotational nystagmus, within certain limits, represents a reaction to the amount of rotation seems of special importance. During rotation these movements of the eyes dissect the panorama into a series of pictures, each of which is exposed to the retina for a moment. We know that the retina reacts for a certain time to every beam of light, so each picture must be fixed long enough to avoid confusion with the after-excitation of earlier images and with the excitation of the next. The gap between the separate pictures is compensated by the fusion of a series of images exposed one after another into the perception of "movement," the principle on which cinematography depends. Without nystagmus the objects could not be fixed long enough to leave a sharp picture on the retina; vision would be indistinct and points would appear as lines whenever we rotated.

Our experiments seem to suggest that the number of pictures into which the panorama is divided during rotation does not vary much at different speeds. The teleological aspect of the problem allows one to

predict that this will not be true with greater speeds of movement. There is an "upper limit" of the latency of the nystagmus jerk adapted to the duration of the after-discharge of the retina. If the interval becomes shorter than this we would get double and triple pictures of moving objects, just as one does when moving objects are illuminated with a spark. This, as a matter of fact, seems to happen under pathological conditions only.

7·5 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	4			4			Feb. 7
180°	9			9			,, 12
360°	15	1		16	1		,, 12
2	8	7	4	14	5½	6¼	Mar. 14
3	3¼	3	2	4	5	3	,, 14
4	6½	5⅝	5	4	4½	4	,, 16
5		6	5½		8½	6½	,, 15

10 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	3			4			Feb. 7
180°	7	(1)		7	(1)		,, 7
1	11	2		10	2		Mar. 14
2	13½	6½	4	14	7½	5	,, 14
3	12½	7	5½	11½	6	4⅞	,, 14
4	3	3	3	4	5	5	,, 16

15 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	3			3			Feb. 7, 1927
180°	6½	(1)		6½	(1)		,, 7, 1927
360°	13	(1)		13	(1)		Mar. 12
2	14	5¼	4½	16	5	4½	,, 14
3	13	7½	4½	13½	9⅛	5⅝	,, 14
4	9	7	6½	8⅝	6⅝	7	,, 16
5		7½	5⅝		8	6½	,, 12
10		8⅝	6½		10⅞	8	,, 15
20		8	6		7	6½	,, 15

20 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°					(1)		
180°	3½	(1)		4	1		Mar. 14
360°	6	1		7	4		,, 14
2	13	3½	2	13	7⅕	2⅕	,, 14
3	15⅗	5	2⅗	15⅗	9¾	4½	,, 14
4	13	9	7	11⅕	10⅗	8	,, 16
5		10⅗	7⅕		13⅕	7½	,, 15
10		10	8⅗		13	8½	,, 15
20		12½	9			9½	,, 15
40							

30 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	5			7			Feb. 7
180°	6	(1)		6	(1)		,, 12
360°			3			4	Mar. 12
2	11⅕	5	5	12½	6	6	,, 14
3	13½	6	5½	13⅖	8⅕	6⅘	,, 14
4	12⅕	8⅕	7⅕	13½	10	7	,, 16
5		13	8½		11⅖	10	,, 15
10		16	10½		17¾	12	,, 15
20		17	12		21	12½	,, 15
40							

60 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°							
180°							
360°		1½	2		1½	2	Mar. 16
2		4	3¾		4	4½	,, 16
3		6½	5½		7	5½	,, 16
4		8¾	6¾		10	6¾	,, 16
5		12⅕	7½		12⅕	7½	,, 15
10		21	10¼		21⅖	10½	,, 15
20		27	14		30	14	,, 15
40		47	18		43	19	,, 16

Electrical Excitation of the Remaining Brain (March 18, 1927).

The animal received 0·45 gr. of bulbocapnine hydrochloride subcutaneously; later in the course of the operation 0·04 gr. was given; the scalp was infiltrated with 1 per cent. novocain solution and the skin was cut in an X-shaped incision. The temporal muscles were separated easily on both sides from a dura-like connective tissue membrane which

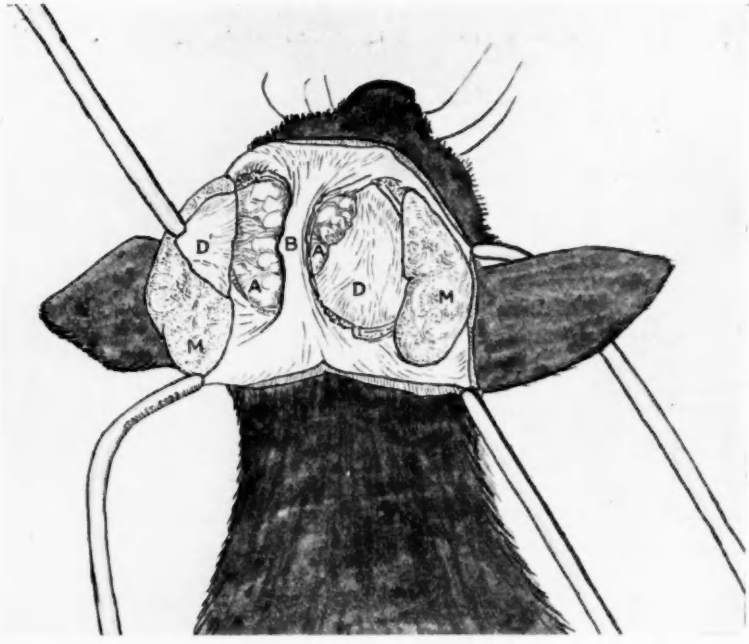

Fig. 9.—Appearance of the skull and of the brain at the first stage of the biopsy. A, arachnoidal cyst. B, arch of bone. D', the dura which has been reflected back. D, dura in place as exposed. M, muscle which has been dissected from the skull.

was adherent to the longitudinal bridge of bone which was left at the former operations; it was dissected from this bridge. After this a transparent cystic mass which contained fluid appeared on both sides of the bridge. This apparently consisted of dilated arachnoidal spaces filled with cerebrospinal fluid. Nervous tissue could be seen in the floor of these cysts. The dura was lightly attached to the walls of the cysts,

but could be separated from them (fig. 9). The bridge of bone was then removed, and below it a thick band of connective tissue, which corresponded to the sagittal sinus and falx, was found. This band was dissected at the frontal end, and carefully reflected towards the occipital bone. The cysts on both sides collapsed owing to small punctures in the arachnoid. The arachnoidal tissue was incised and this exposed two huge cavities with flat walls. The last part of the operation had to be performed under ether anæsthesia, as the cat became very restless whenever the dura-like membrane was touched. The entire operation lasted an hour and a half.

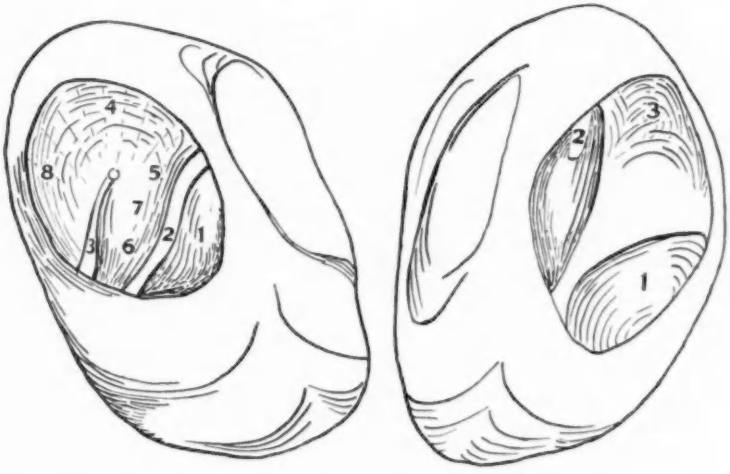

FIG. 10 (Compare with fig 11A).—These drawings of the cysts show the areas which were stimulated and later identified by microscopical examination.

A sponge soaked with saline was placed in each of the open cysts. Between noon and 2.30 p.m. the animal gradually recovered; at 2.30 she was able to walk fairly well. She was hung in a towel in which holes had been cut for the four extremities; the electrical stimulation was then begun. Periodic motor discharges were observed, independent of electrical excitation; these were accompanied by dilatation of the pupils and acceleration of the respiratory rhythm. Tremors also appeared spontaneously from time to time.

Reactions to Electrical Stimuli (compare fig. 10).

2.45 p.m.—Animal hanging in the towel. Making slow walking movements with her forepaws; claws expanded on all four legs; head turned to left; respiration rapid, 48.

2.29 p.m.—Wound is opened. Removal of cotton from right cyst. Alternating movements of forelegs.

2.31½ p.m.—Stimulation of posterior part of mesial wall of right cyst; 10 cm. distance of coils. Alternating movements of forelegs; more tonic extension of right leg.

2.33 p.m.—Stimulated again: nothing new.

2.34 p.m.—Stimulated with coils 7 cm. apart; no reaction.

2.35 p.m.—Stimulated on outer surface (point 1).

2.36 p.m.—Stimulated anterior to point 1; no change.
Later tonic reaction, turning head to right.

2.40 p.m.—Point 1; winking movements of both upper lids, especially left, a short time after stimulation.

2.42 p.m.—Point 1; tonic turning of head to right.

2.42½ p.m.—Point 1; winking of both upper lids, and as an after-effect tonic turning of head to right and high stepping of forelegs.

2.43 p.m.—Stimulated again. Point 1; winks both upper lids.

2.44 p.m.—Stimulated again. Point 1; winks both upper lids.

2.48 p.m.—Stimulated Point 2 (9 cm.) in anterior part of middle of mesial wall of right cyst; deep and rapid breathing.

2.49 p.m.—Same.

2.50 p.m.—Stimulated Point 2 (13 cm.); no reaction except movement of foreleg.

2.52 p.m.—Stimulated Point 2 (10 cm.); urination.

2.53½ p.m.—Stimulated Point 2 (9 cm.); superficial and rapid respiration; urination (this continued a few seconds after stimulation).

2.54 p.m.—Stimulation repeated; deep, long respiration.

2.56 p.m.—Stimulation repeated; increased respiration and a good deal of movement.

2.57 p.m.—Stimulation of Point 3 (9 cm.) in anterior end of cyst; no effect.

2.57½ p.m.—Stimulation of Point 3 (9 cm.) in anterior end of cyst; no effect.

On handling head afterwards (raising chin), marked tremor of both forelegs.

2.59 p.m.—Stimulation of Point 3 (9 cm.); the right leg twice made long goose-step movements. More movements half minute afterwards.

3.1 p.m.—Touching head to sponge out cyst; increased respiration.

3.1½ p.m.—Stimulation of Point 2; rapid respiration.

3.2½ p.m.—Stimulation of anterior end of mesial wall; no effect.

3.3½ p.m.—Stimulation (9 cm.) of anterior end of lateral wall; alternating movements of forelegs and more rapid breathing.

3.5 p.m.—Repeated, same results.

3.6 p.m.—Raising head without stimulation causes a few movements.

3.6½ p.m.—Further raising of head, same result.

3.7 p.m.—Stimulation of anterior part of mesial wall; movements of forelegs immediately.

3.8 p.m.—Stimulation of Point 1; winked once; tonic turning of head to right.

3.8½ p.m.—Stimulation repeated; no winking, but moving of legs and turning of head to right.

After effects: more running movements of legs than before stimulation.

3.11 p.m.—Stimulation of Point 1 (9 cm.), several times; alternating movements of leg; head turned to right; right hindleg moved a few times.

3.13½ p.m.—Stimulation of Point 2 for 25 sec.; increased respiration. After-effect: two squawks.

3.14¾ p.m.—Stimulation of Point 2 twice in succession; no effect.

3.16 p.m.—Stimulation of anterior part of mesial wall for 15 sec.; no change in legs.

3.16½ p.m.—Stimulation of Point 1; slight winking of eyes.

3.16¾ p.m.—Same, repeated 3-4 times; same results. After effects—spastic stepping movements; no turning of head; marked walking movements of forelegs.

3.18 p.m.—Stimulation same; no results while the current was on. After-effects same as above.

3.18½ p.m.—Stimulation of Point 1 (9 cm.); nothing. After-effects: running movements; lifts legs as high as nose; cried.

3.20 p.m.—Stimulation same; rapid respiration.

3.22 p.m.—*Left* cyst opened and right one closed with plug of cotton-wool. High reaching with forepaws; head to left; tremor.

3.24½ p.m.—Stimulation of Point 1 behind posterior wall of cyst (9 cm.); high stepping and head turned to left.

3.25 p.m.—Stimulation same; no effect; cried afterwards.

3.27 p.m.—Stimulation of Point 2 (9 cm.) on medullated line on floor of left cyst; licking movements; left facial contractions; puckering of nose.

3.28 p.m.—Stimulation same; previous movements repeated. After-effects (1 min.): epileptic attack; tongue to left; biting movements; salivation; head to left; tongue in and out.

Separation of coils to 12 cm.

3.31½ p.m.—Stimulation of anterior part of bundle; forepaw flexed.

3.32 p.m.—Stimulation of posterior part of bundle; no effect.

Coils again separated to 9 cm.

3.33 p.m.—Stimulation of anterior part of bundle; licking and movements of mouth.

3.34¼ p.m.—Stimulation of posterior part; licking in midline.

3.34¾ p.m.—Stimulation of anterior part; movement of nose; tongue out in midline. After-effect: became sleepy.

3.36 p.m.—Stimulation repeated; left lip moved first and then right lip.

3.37 p.m.—Stimulation in angle between anterior wall and floor of cyst; no effect on legs; respiration a little more rapid. Repeated with same results.

3.41 p.m.—Stimulation of Point 3; cried once; respiration more rapid; both eyes moved down.

3.41½ p.m.—Stimulation repeated.

3 p.m.—Repeated.

3.47 p.m.—Stimulation of Point 4 in roof of cyst: no effect (perhaps slight jerking of eyes).

3.49 p.m.—Stimulation of Point 5 (mesial part of grey mass on floor); animal absolutely quiet. After-effects: few licking movements; turned head to left; stepping a little.

3.51 p.m.—Stimulation repeated; stepping movements; cried; pupils dilated.

3.52 p.m.—Stimulation repeated; turns head far to left.

3.53 p.m.—Stimulation repeated. After-effects: running movements and elevation of head.

3.54 p.m.—Stimulation of Point 6 (lateral part of grey mass): twitching of left side of face; left eye winked (at this point a slight hæmorrhage occurred); increased respiratory rate.

3.54½ p.m.—Stimulation repeated; same results. Afterwards: running movements.

3.56 p.m.—Stimulation of Point 7 (between 5 and 6); very rapid breathing, with nostrils moving.

3.58 p.m.—Stimulation repeated. Afterwards: breathing stronger and dilatation of nostrils.

3.59½ p.m.—Stimulation of Point 8 (anterior lateral wall of cyst). Afterwards: running movements.

4.1 p.m.—Stimulation same.

4.2 p.m.—Stimulation of Point 6; contraction of muscles of left side of face.

4.4 p.m.—Stimulation of Point 5; a few jerks of both eyes to left.

4.5 p.m.—Repeated. Results same.

4.5½ p.m.—Repeated. Movements of head and eyes to left; left eye-jerks. Afterwards: running movements and head turned from right to left.

4.7 p.m.—Stimulation of Point 5 twice; eyes jerked.

Stimulation of Point 5 twice; eyes jerked to left. Afterwards: running movements and cried once.

4.9¼ p.m.—Stimulation same; eyes jerk downwards.

4.12¼ p.m.—Stimulation of Point 6; no effect.

4.13½ p.m.—Stimulation of lateral part of Point 1; no effect.

4.15 p.m.—Stimulation of Point 7; no effect.

4.16½ p.m.—Stimulation of Point 2; left whiskers moved; both lip whiskers changed a little. Afterwards: constriction of both pupils; head rigid.

4.17½ p.m.—Stimulation repeated; champing; tongue moved in and out in midline; whiskers moved. Afterwards: quite rigid.

Returning to Right Cyst.

4.21¼ p.m.—Stimulation of Point 1; no results.
4.21½ p.m.—Repeated. Winking.
Repeated. Winked with left eye.
Repeated. No result.
4.22½ p.m.—Stimulation of Point 2; increase in rate of respiration.
4.25 p.m.—Stimulation of Point 2; marked increase of respiration.
4.26 p.m.—Stimulation same. Not much change.
4.26½ p.m.—Stimulation same. Not much change. Afterwards: strong running movements.
4.27½ p.m.—Stimulation repeated. No result.

Returning to Left Cyst.

4.36½ p.m.—Stimulation of Point 2; whiskers moved; licking; champing: movement of tongue.
4.38½ p.m.—Stimulation of Point 2 (increased current). Champing licking, &c. Afterwards: licking, head turned to left.
4.40 p.m.—Stimulation same. Champing and licking. Spot marked with indian ink.

Return to Right Side.

4.55 p.m.—Stimulation of Point 2. Increased respiration. Spot marked with indian ink.

Summary of Excitation Experiments.

In studying this protocol one must take into consideration the fact that periodic discharges of movements took place, a typical phenomenon in cats without the forebrain when they are suspended, as Schaltenbrand and Girndt [17] have shown. These movements may have started by chance, or as the after-effect of electrical stimulation of any point, so they cannot be considered as a definite effect. Twitching of the eyelids and of the face could be elicited behind the right cornu Ammonis; it is doubtful if these were of reflex origin (due to trigeminal irritation) or a result of spread of the electric current to the base of the skull. The animal had also a tendency to rotate its head more frequently to the right while we were working on the left side of the brain.

Definite effects could be obtained from "Point 2" on the left side, which lay over a medullated bundle running to the midline. When this bundle was stimulated the nose was puckered, the

whiskers moved, the animal made biting, licking and swallowing movements, and stronger stimulation excited epileptic attacks. Another area from which definite effects could be obtained was "Point 2," on the velum medullare of the right ventricle. Excitation of this point was twice followed by evacuation of the bladder, and repeatedly by irregular changes of the respiratory rhythm.

At the end of the experiment the animal was able to stand and to walk; she was unsteady, however, and more tremulous than usual.

Necropsy.

When the experiments were completed the animal was anæsthetized with ether and was bled from the femoral arteries. While the heart was still beating the carotids were injected with formalin.

The spinal cord was removed within the dura and left attached to the medulla oblongata. The head was then severed from the atlas. Sponges soaked in formalin were introduced into the cysts, and the head and spinal cord were put into formalin.

On March 20 the bone was removed from around the brain. The pieces of muscle which had been inserted at the operations were densely adherent to the dura, and between them and the cortex there was a reddish mass of jelly-like consistency. The brain was removed easily without damage. The middle ears and labyrinths appeared normal to the naked eye.

Description of the brain (fig. 11).—Some cortex had been left, including on the left side the gyrus proreus, most of the lobus piriformis and a small part of the gyrus fornicatus; and on the right the gyrus proreus, the entire lobus piriformis and the edges of the gyrus ectosylvius and gyrus fornicatus. The cornu Ammonis was visible on both sides. On the left side the choroid plexus could be recognized. The anterior and posterior horns of the lateral ventricles were represented by large cavities. The stimulation experiments had been made in the anterior horn of each ventricle. On trying to lift up some overhanging tissue from the posterior end of the left anterior horn, the brain was torn slightly. The right olfactory bulb had been damaged during dissection.

After being hardened in formalin and alcohol the brain was embedded in celloidin and cut in serial sections. Every fourth section was stained by Nissl's method, and every other fourth section by Weigert's method. The serial sections, which were made by an inexperienced technician, were not perfect, but were sufficiently good for the study of the brain. The sections and the photographs do not bear their serial numbers, but the corresponding Nissl and Weigert sections always bear the same number.

Microscopical Examination of the Brain.

The first sections pass through the olfactory bulbs and the frontal poles of the brain. The olfactory bulbs are well preserved, but there are central

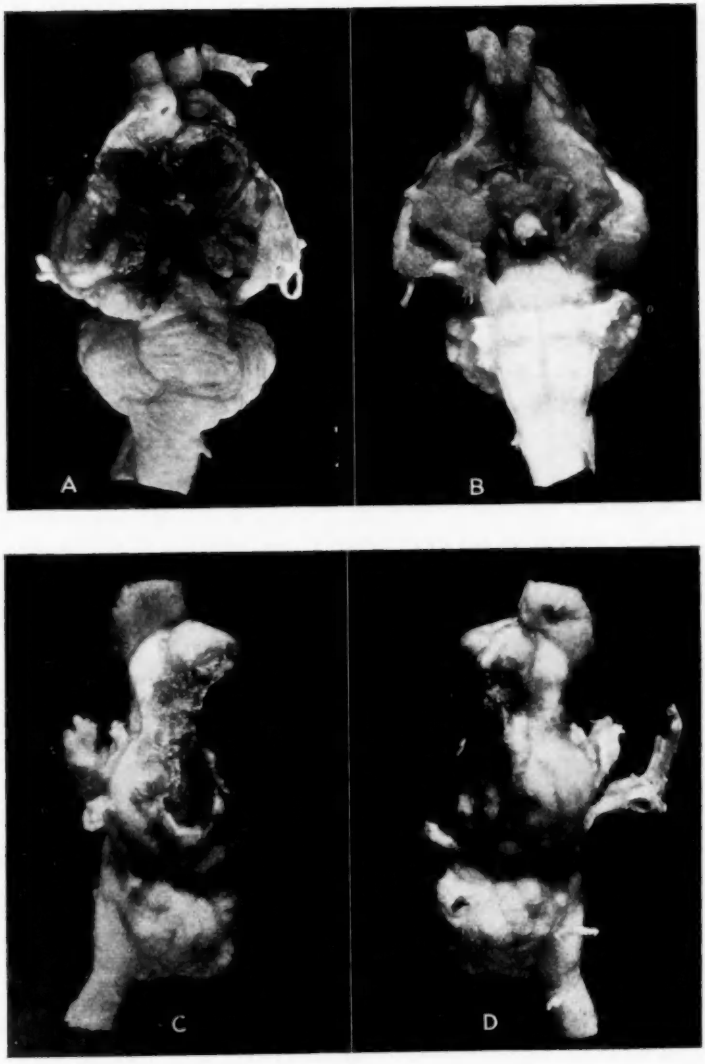

FIG. 11.

softenings around their ventricles. The right frontal pole is larger than the left. The white matter is necrotic and contains cavities which separate the medial and the lateral parts of the cortex.

Section 43 corresponds approximately to plates 1 and 2 of Winkler and Potter's monograph. A good deal of cortex remains in the frontal lobes of both sides, especially in the gyrus proreus and gyrus genualis (fig. 12 Nissl stain). The operative incision followed the sulcus Sylvii and the sulcus cruciatus, leaving only a small part of the gyrus sigmoideus anterior. The cortical cells are well preserved, and a few pyramidal cells can be recognized on both sides. The large cells in the sixth layer have disappeared on the left side, which was operated on first, but are still present on the right. The meninges are infiltrated by cells. Weigert's stain shows that the white matter has

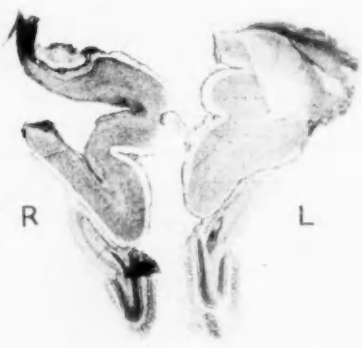

FIG. 12.

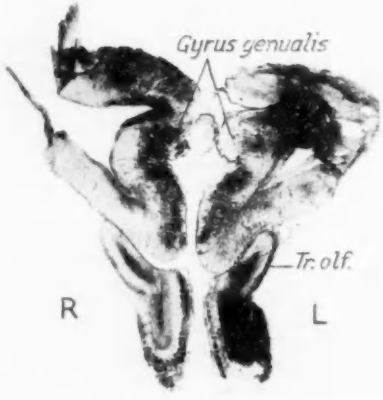

FIG. 13.

disappeared on both sides with the exception of a few arcuate fibres (fig. 13). In both hemispheres the operation has entirely destroyed all fibres which might pass around the ventricles to enter the internal capsules.

Section 60, Nissl stain, shows the brain a little anterior to the genu of the corpus callosum. A necrotic mass of fibres on both sides corresponds to the commissural radiation from the corpus callosum. The only cortex remaining is a small portion of the gyrus rostralis above this mass and the gyrus genualis below it. The olfactory tract, which has united with the brain, is well preserved on both sides. On the left side a small portion of the area 13 of Winkler and Potter remains in the depth of the sulcus præsylvius, but on the right there is only a very thin layer. Some large cells above this layer might correspond to the oral part of the claustrum. The caudate is not yet visible, and there is no indication of the capsular radiation of the frontal cortex. In the Weigert sections the tapetum appears degenerated.

Section 78 passes through the necrotic genu of the corpus callosum (fig. 14, *G. c.c.*), which is collapsed and folded; below it a dark line of cells on both sides represents the nucleus medullæ terminalis. On the right side the pole

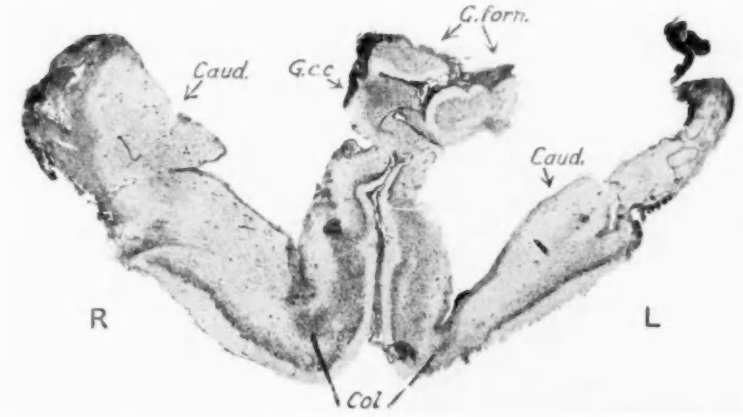

FIG. 14.

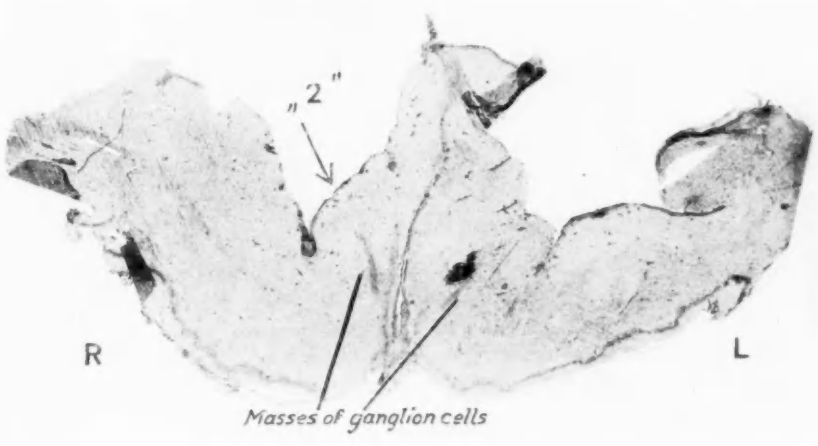

FIG. 15.

of the caudate is separated by the necrotic internal capsule from what seems to be the putamen. A few myelinated fibres in the capsule belong to the striothalamic radiation. The parts of the cortex preserved are the same as in the more anterior sections. Laterally the brain extends out on each side to

the necrotic gyrus orbitalis. The anterior end of the striatum is preserved to a great extent on the right side, but on the left the caudate only can be recognized. The colliculum striati (*Col.*) is well developed on the right.

Section 98 (fig. 15, Weigert; and fig. 16, Nissl) shows the radiation of the olfactory medulla forming the anterior part of the anterior commissure. An increasing number of medullated fibres is seen in the right internal capsule; they apparently radiate from the well preserved striatum and also from the posterior part of the gyrus orbitalis, which is also preserved. The striatum is bordered by a line of necrosis on both sides. The ganglia olfactoria Luysii are

FIG. 16.

well developed. The septum and the striata contain old organized tissue and fresh hæmorrhages, the latter apparently due to mechanical irritation during the electrical stimulation. There is a symmetrical nucleus situated in the radiatio olfactoria medialis on both sides which is not mentioned in Winkler and Potter's "Atlas," but can be found in the normal cat series which has been used for comparison (fig. 16). Above the right nucleus, on the velum medullæ, are a few spots of indian ink, representing "Point 2" (see fig. 15, "2"), Stimulation of this point gave rise to urination and changes in the respiratory rhythm.

Section 113 (fig. 17) shows a considerable increase in the radiatio striothalamica (*R. Str. th.*), in the right internal capsule and in the anterior

commissure (*Ant. comm.*) on both sides. On the left side, where the caudate (*N. caud.*) is less well preserved, a bundle of the radiatio striothalamica appears. The gyri fornicati (*G. forn.*) and corpus callosum (*Corp. Call.*) are seen above, and below the fibræ rhinencephales mammillares (*F.R.M.*) and the

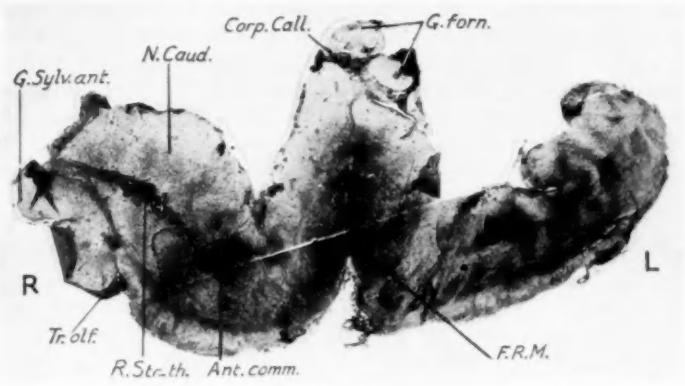

FIG. 17.

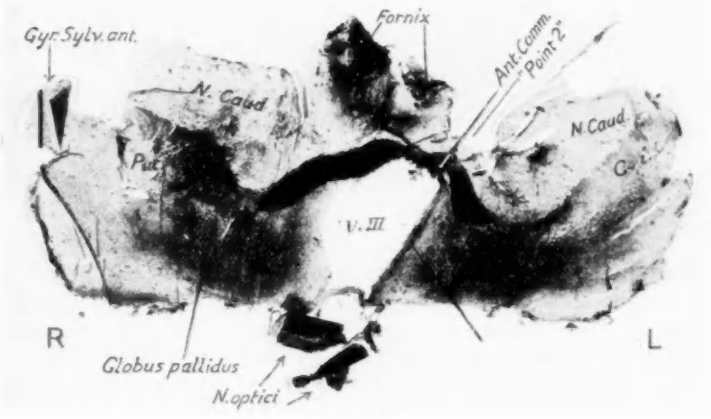

FIG. 18.

tractus olfactorius (*Tr. olf.*). On the extreme right is the gyrus Sylvius anterior (*G. Sylv. ant.*).

Sections 119 to 137 contain the well-developed anterior commissure. In all these sections some indian ink can be seen on the floor of the left ventricle just above the anterior commissure; it corresponds to "Point 2," from which

licking and swallowing movements, puckering of the nose and epileptic attacks could be obtained by a faradic stimulation.

In section 134 (fig. 18, Weigert) the anterior commissure divides the specimen into an upper and a lower part. The upper part consists of the anterior end of the fornix, which still contains some fibres, and the caudate nuclei. Laterally the internal capsule (*C. i.*) joins the anterior commissure. Below the anterior commissure there is a large open space, the hydrocephalic third ventricle (*V. III.*) The globus pallidus and the anterior end of the nucleus amygdalæ can be seen. As in all sections, the right hemisphere is better preserved than the left and still contains the tractus olfactorius and a small portion of gyrus Sylvius anterior (*Gyr. Sylv. ant.*), both of which are absent on the left side. The optic nerves appear at the base (*N. optici.*).

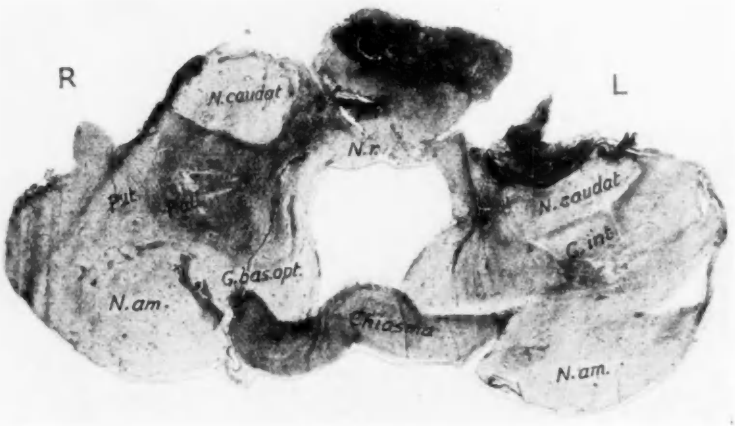

FIG. 19.

In sections 137-143 the choroid plexus is seen above the fornix. No part of the gyrus fornicatus remains. Below the anterior commissure the prethalamic nuclei can be seen; the nucleus filiformis is almost completely degenerated on the right side but is well preserved on the left. The contrast is especially marked in section 143. The first cells of the ganglion basale opticum appear.

Section 158 (fig. 19, Weigert) shows the nuclei caudati very well, especially in the Weigert preparations. The left nucleus is collapsed and has assumed a semilunar appearance owing to the deformation of the hemisphere. The ganglion habenulæ can be recognized. The chiasma is cut across and the optic tract enters the brain on both sides. The lateral and medial nuclei of the thalami are atrophic, but this is more evident in more posterior sections. The left thalamus is affected more severely than the right. On the right side

the claustrum, nucleus amygdalæ, putamen and pallidum can be recognized; on the left side the putamen is deformed and the claustrum is absent. On the right side the cortex includes the frontal end of the gyrus Sylvius posterior and a small part of gyrus Sylvius anterior; on the left side only a part of the lobus piriformis remains. The medullated fibres on the upper surface of the temporal lobe belong to the stria terminalis.

Section 180 contains the pituitary gland and the anterior part of the degenerated left lateral geniculate body. The thalami are united by the massa intermedia. The fasciculus fornicis and the bundle of Vicq d'Azyr can be seen on both sides. The nucleus reuniens still contains a number of cells, and a

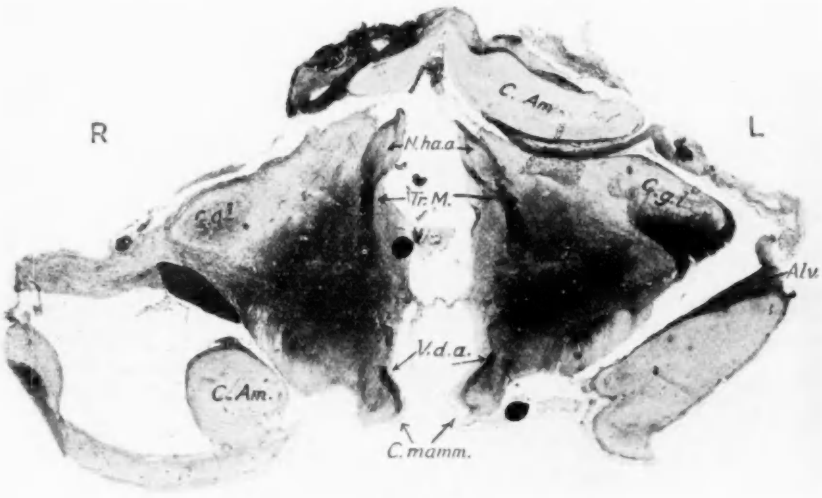

FIG. 20.

few groups of cells remain which might correspond to *Mc* and *Va*. The nuclei filiformes are equally developed on the two sides.

Section 193. The thalami are separated again, the right is better preserved than the left. The anterior end of each cornu Ammonis appears, and the left optic tract enters the lateral geniculate body. The posterior horns of the ventricles are very hydrocephalic, and that of the left is open laterally.

Section 206 (fig. 20) shows Meynert's tracts descending towards the base of the brain. The fasciculi of Vicq d'Azyr (*V.d.a.*) enters the mammillary bodies. The pyramidal tracts are completely degenerated in the pedunculi cerebri. The fibres of the substantia nigra and the other parts of the hypothalamus are well preserved. The left corpus geniculatum medialis can be recognized. The left fimbria is present, and the alveus (*Alv.*) is visible in each cornu Ammonis (*C. Am*). Only a few cells remain in the lateral geniculate body.

(*G.g.l.*). The nucleus parependymalis is well developed on both sides. The rest of the thalamus is degenerated and contains only a few cells, most of them grouped around Meynert's tract.

Sections 215-224 cut across the aqueduct of Sylvius and the anterior end of the posterior commissure. The optic tract enters the lateral geniculate body on the right side. The fibres of the pedunculus corporis mammillaris can be recognized. The pulvinar and the nucleus posterior thalami are completely degenerated.

Section 222 (fig. 21) shows the extent of the cortex which has been preserved; with the exception of the cornu Ammonis only the lobus piriformis remains. The structure of the different cell layers is the same on both sides.

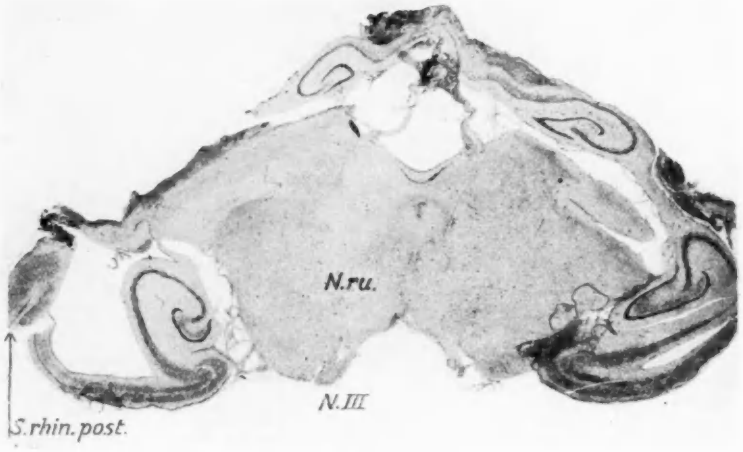

FIG. 21.

On the left side the cortex ends approximately between fields 28 and 35 (see Winkler and Potter). On the right side a part of the gyrus Sylvius posterior, containing part of area 35, is preserved. The third nerve (*N. III*) is cut across. The lateral geniculate body contains only glia. The medial geniculate body can now be recognized on both sides, but it contains only a few scattered cells. The optic radiations are completely degenerated. A good many cells remain in the region of the nucleus posterior thalami and in the pulvinar. The groups of cells around Meynert's tracts are well preserved. In section 224, Meynert's tracts are seen between the oculomotor nerves (see fig. 22).

In section 235 the red nucleus (*N. ru.*) and the substantia nigra appear normal. The medial geniculate body has disappeared on both sides. The brachium of the right posterior quadrigeminal body is severely degenerated. Neither peduncle contains medullated fibres, and the left is shrunken more than

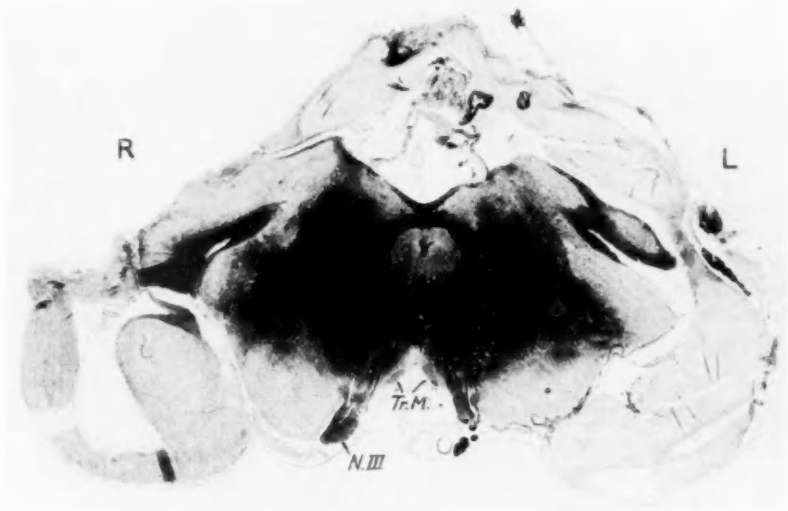

FIG. 22.

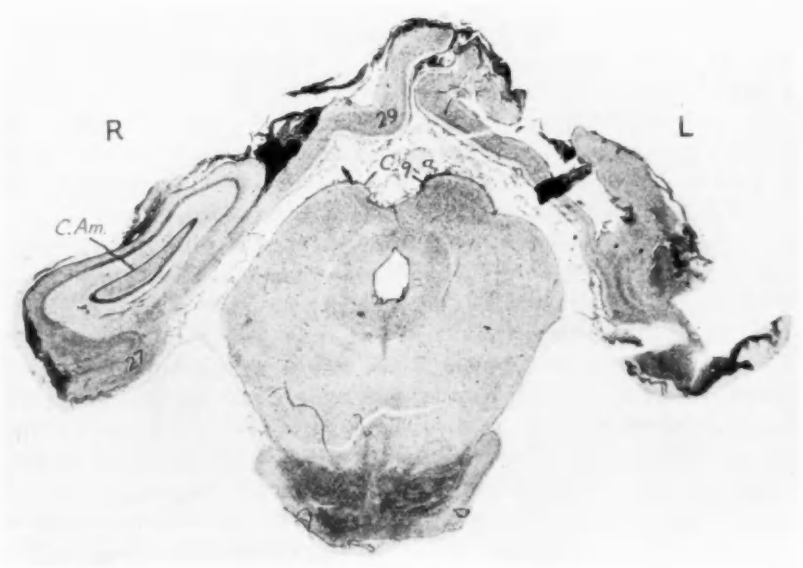

FIG. 23.

the right. Each cornu Ammonis contains a thin layer of medullated fibre. The lobus piriformis is still preserved.

Section 264 (fig. 23, Nissl) shows more cortex than the previous ones. The area 29 of the gyrus fornicatus is well preserved on both sides; some necrotic tissue from the adjoining areas is visible on top of it on the left side.

In Section 273 the chief abnormal feature is the degeneration of the brachium of the right posterior quadrigeminal body which seems to be due to a small area of necrosis in the lateral aspect of the quadrigeminal body. This necrosis can be recognized still better in section 286.

Section 278 shows even more cortex preserved. On the left side is the sulcus splenialis, a small piece of the gyrus splenialis posterior and the gyrus splenialis. The cortex covering this is not of the structure of area 17, but from its position must correspond to it. No medullated fibres remain in this region.

In sections across the pons and the medulla the pyramidal tracts are completely degenerated.

Summary of the Anatomical Findings.

More of the right side of the brain remained than of the left. Small portions of the convolutions which border the rhinencephalon were preserved on the right side, while on the left the operative incision followed almost exactly the sulcus præsylvius, the sulcus rhinicus anterior and the sulcus rhinicus posterior, so that even the lobus piriformis was removed and the olfactory tract was damaged. The subcortical ganglia were well preserved on the right side, but on the left the head of the caudate nucleus and the putamen were injured, and the claustrum was almost completely destroyed. The nucleus amygdalæ was intact on the right, and a considerable part of it remained on the left.

Some of the neocortex was preserved, chiefly in the frontal lobes. On both sides the gyrus proreus, the gyrus genualis and parts of the gyrus sigmoideus anterior and gyrus præsylvius remained. The anatomical examination showed, however, that with the exception of the gyrus proreus and gyrus genualis this neocortex must have been functionless, as its medullary layer was necrotic and the operative incision passed so far frontally that all the pyramidal fibres running around the ventricle were destroyed. On following the serial sections backwards the neocortex rapidly diminished, and when the genu of the corpus callosum was reached only a small piece of the gyrus rostralis was left. The genu, which is the only part of the corpus callosum which remained, was necrotic.

It is interesting that there were a number of myelinated fibres in each internal capsule, especially in the right. The study of the serial sections shows that these fibres were extrapyramidal, connecting the head of the caudate nucleus and the putamen with the lower parts of the basal ganglia. They correspond to the well-known radiatio striothalamica described by Rothmann [16], Dresel and Rothmann, Brouwer [4], Ferraro [7], and Karplus and Kreidl [9] in their decorticated animals. A small number of fibres in the right internal capsule may represent a radiation from the edge of neocortex which remained along the right rhinencephalon. That the internal capsule contained no pyramidal fibres was evident from examination of the mesencephalon, as here both peduncles are completely degenerated.

A good deal of cortex remained in the occipital poles. Area 29 (gyrus splenialis posterior) was well preserved, and small portions of the neighbouring cortex (areas 17 and 18) persisted on the left side, but they had lost their typical structure. Area 29 was probably functional as it was connected with the still medullated alveus. A study of the serial sections shows complete absence of the optic radiations, so the small remnant of the visual area (areas 17 and 18) cannot have had any fibre connections with the lateral geniculate body.

In places the injury was asymmetrical : for instance, the left nucleus filiformis was degenerated, while the right was well preserved. As the third ventricle was opened widely during the second operation, it is not impossible that this nucleus was damaged mechanically. A similar lesion to the right posterior quadrigeminal body probably explains the degeneration of the right posterior brachium.

While the hypothalamus seemed to be in a good state of preservation, the thalamus had undergone severe degeneration. The study of this series of sections confirms fully the findings of v. Monakow [14], Nissl [15], Brouwer [4], and others. The anterior and lateral parts of the thalamus were most severely affected, only the nucleus reuniens, the nucleus habenulæ, the nucleus parependymalis and the tract of Meynert escaped. The medial parts of each thalamus were better preserved. Only a few scattered cells remained in the nucleus centralis, nucleus posterior and in the pulvinar. The degeneration of the medial parts of the thalami was about the same on the two sides. The nucleus filiformis had disappeared on the side where the striatum was best preserved. The ganglion geniculatum laterale was also degenerated and contained only a few cells near the entrance of the optic tract.

The great majority of the cells of the ganglion geniculatum mediale had disappeared.

It is important that the thalamus was better preserved on the side where the striatum was intact. This indicates that some of its cells are connected with the striatum, though most of them are connected with the cortex.

Two of the points which were stimulated electrically could be located as they were marked with indian ink. On the left side "Point 2" lay on the anterior commissure. On the right side "Point 2" lay on the velum medullare anterior, above a comma-shaped nucleus of small cells which is found also in a normal cat.

Summary of Physiological Observations.

A review of the protocol of the animal "Kleopatra" shows that she possessed all the functions described by other observers in animals after removal of the forebrain, and in addition other functions not previously described. These were:—

(1) The elaborate mechanism which cats employ to keep their fur in good condition.

(2) A shaking reflex of the extremities, which was especially active during the first days after operation. These shaking movements could be regularly elicited by putting the paws into some sticky solution; immediately after the operation, though the limbs were weak, this reflex was so active that it developed spontaneously as soon as the animal placed her feet to the floor. This observation suggests that there was something in common between the movements of the partially paralysed limbs and the movement of a limb soiled with a sticky fluid.

(3) A state of hyperexcitability. This decorticated animal, in which the striatum was almost intact, was in a peculiar restless state for a prolonged period, especially when she was irritated by intercurrent infections.

(4) Polydipsia, polyuria and polyphagia immediately after the second operation. The only anatomical finding which can be brought into relation with this observation is the almost complete degeneration of the nucleus filiformis in the wall of the third ventricle on the left side.

A comparison of the electrical stimulation experiments with the anatomical findings gives two new results:—

(1) The production of smelling, licking and swallowing movements, and of epileptiform fits, by stimulation of the anterior commissure.

(2) Evacuation of the bladder and a change in respiratory rhythm on stimulation of the septum medullare anterior in the region of a comma-shaped nucleus. This nucleus consists of small cells; it is found in normal cats, but does not appear to have been previously described.

The other results of stimulation were indefinite and varied so much that it is difficult to attribute any value to them. The two positive results are conclusive, for we used bipolar stimulation, the reactions were very sharply localized, and the previous operations had produced complete degeneration of the radiations from the frontal neocortex.

A comparison of the behaviour of the thalamus cat and the striatal cat is not entirely satisfactory, because the thalamus cat lived for such a short time. It points, however, to the conclusion which has already been drawn by Dresel and Rothmann [16] that striatal animals have a wider range of motor activity and greater variation of behaviour than thalamic animals. The thalamus cat with its permanent, dull circus movements gave the impression of an automaton, while the striatal cat, even a few days after the operation, displayed a much greater variety of speed, direction and modification of gait, and responded more readily to auditory and sensory stimuli.

Summary.

Two cats without neocortex are described clinically and anatomically. In the first both cerebral hemispheres were removed anterior to the thalamus; this animal lived for nine days after the second operation. It exhibited states of waking and sleep, and when awake it made purposeless circus movements. It did not eat spontaneously.

In the other animal the rhinencephalon and striatum were left intact; this animal was kept alive for five months after the second operation. Immediately after the second operation it showed much more activity and a greater variety of movements and of reactivity than the thalamus cat. It reached and ate its food spontaneously, and for a time it had polydypsia, polyphagia and polyuria, which were probably due to destruction of the right nucleus filiformis. Immediately after the operation the animal developed a well-marked shaking reflex of the extremities; this was shown to be an exaggeration of the normal shaking reflex which serves to clean or dry the paws. The animal cleaned its fur spontaneously. Its motor activity, when recorded in an "activity

cage," was found to be much greater than that of a normal cat. This excessive activity was excited by noise, and increased during infection by nematodes and mange.

Rotational nystagmus and after-nystagmus were studied on a rotating wheel, and were shown to follow the same rules as in intact animals and in man. As long as the speed and the amount of rotation were kept within physiological limits, the number of jerks depended chiefly on the degree of rotation. On longer rotation the after-nystagmus assumed the characters of a reaction to acceleration.

Electrical stimulation, immediately before the animal was killed, of those portions of the brain which remained revealed two points which were definitely excitable. The first proved to be the anterior commissure; stimulation of this produced movements relating to smelling and eating, as puckering of the nose, licking, moving the whiskers and chewing. The second point lay above a small comma-shaped nucleus in the velum medullare; stimulation of it gave rise to urination and changes in the respiratory rhythm.

The anatomical examination showed that, on the whole, the aim of the operations had been attained; the few portions of the neocortex which had been left had no fibre connections with the brain-stem.

The anterior and lateral parts of the thalami had undergone severe atrophy. This atrophy was more marked on the left side on which the striatum had been damaged.

REFERENCES.

[1] Bárány, R. *Monatsbl. f. Ohrenheilk.*, 1907, **41**, 477.
[2] Bard, Phillip. *Arch. of Neur. and Psych.*, 1929, **21**, 230.
[3] Breuer, J. *K. Akad. der Wiss. Math. Nat. Classe Sitzungsber.*, 1903, **112**, 315.
[4] Brouwer, B. *Arch. néerlandaises de physiologie de l'homme et des animaux*, 1919, **4**, 124.
[5] Brown, A. C. *Journ. of Anatomy and Physiology*, 1874, **8**, 327.
[6] Edinger, L. "Bau der Nervösen Centralorgane." Leipzig, 1900.
[7] Ferraro, A. "Étude anatomique du Système nerveux central d'un Chien dont le Pallium a été enlevé." Utrecht, 1924.
[8] Holmes, Gordon. *Journ. of Physiology*, 1901-1902, **27**, 1.
[9] Karplus, J. P., and Kreidl, A. *Arch. f. Physiol.*, 1914, 155.
[10] Mach, Ernst. "Grundlinien der Lehre von den Bewegungszentren." Leipzig, 1875.
[11] Magnus, R. "Körperstellung," Berlin, 1924.
[12] Magnus, R., and de Kleyn, A. *Handbuch d. Neurologie des Ohres*, 1923-1924, **1**, 465.
[13] Masuda, T. *Pflüger's Arch.*, 1922, **197**, 1.
[14] v. Monakow, C. *Arch. f. Psychiatr. u. Nervenkrankh.*, 1889, **20**, 714.
[15] Nissl, F. *Arch. f. Psych. u. Neurol.*, 1913, **52**, 867.
[16] Rothmann, H. *Zeitschr. f. d. g. Neurol. u. Psych.*, 1923, **87**, 247.
[17] Schaltenbrand, G., and Girndt, P. *Pflüger's Arch.*, 1925, **209**, 333.
[18] Schaltenbrand, G., and Cobb, S. *Pflüger's Arch. f. d. g. Physiol.*, 1927, **218**, 475.
[19] Winkler and Potter. "An Anatomical Guide to Experimental Researches on the Cat's Brain." Amsterdam, 1914.

INTRACRANIAL ANEURYSMS.

BY MAX SCHMIDT,

Assistant in the Department for Mental Diseases in the Kommunehospital, Copenhagen.

[From the Psychiatric Laboratory of the University and the Department for Nervous and Mental Diseases in the Kommunehospital at Copenhagen. Chief Professor Aug. Wimmer, M.D.]

CASES of intracerebral aneurysms diagnosed during life must still be regarded as rare, although investigators recently have succeeded in diagnosing leaking or ruptured aneurysms in many cases. It is therefore worth while to see whether on a somewhat larger material diagnosis during life is as impossible as previous investigators (Gull, Beadles, Fearnsides, Wichern, among many others) have indicated. The difficulty appears to have lain in great measure in the fact that the possibility of aneurysm (Wichern) had not been thought of and that the different pictures of the disease were but little known. Intracranial aneurysm is certainly not a common disease, but on the other hand it is not a very infrequent one. In most cases aneurysms have a bad prognosis, especially when once they have begun to bleed, but on the other hand the possibility of effective surgical therapy, once the diagnosis is fairly sure, cannot be altogether excluded. It is therefore tempting to take up the question on a broader basis, especially since a number of questions concerning the ætiology, the pathogeny and the special pathological anatomy of intracranial aneurysms are still far from being answered.

Some case reports of intracranial aneurysms which have shown characteristic pictures by radiograms have appeared recently. These cases, to which I can add a new one, seem to open new diagnostic possibilities.

Having had occasion to observe personally some cases of aneurysm (one of these was diagnosed), I collected from the Department for Nervous and Mental Diseases of the Kommunehospital all the cases in which intracranial aneurysms had been proved by autopsy in the period from 1914 to 1929, both years included. As this material was not primarily examined with a view to scientific publication, it naturally has defects both on clinical and pathologico-anatomical grounds. The histories are

often rather summary, as some of the patients were admitted in a state of coma, and death occurred shortly after. When an autopsy was made aneurysms were not specially sought for, and small aneurysms the size of a mustard grain or even larger may well have been overlooked. Only a few cases which gave no signs of aneurysm during life were found, because autopsies from the other departments of the hospital did not include the skull and brain unless symptoms of intracranial disease had been present. In several cases autopsy was forbidden by the relatives of the patient. The twenty-three aneurysms collected within fifteen years do not therefore express the real frequency of aneurysms. Further, all cases where death did not occur must be deducted, i.e., the cases discharged from the department.

Historical.

The first known description of intracranial aneurysms originates from Biumi in Milan in 1765. In the year 1834 Nebel reported thirteen cases, and Stumpf fifteen cases in 1836. In 1852 Brinton was able to report forty-nine cases (cited by Fearnsides). Gull in 1859 gave a description of the symptomatology of intracranial aneurysms, and has concluded that: "Although we may from the circumstances sometimes suspect the presence of aneurysms within the cranium, we have at best no symptoms upon which to ground more than a probable diagnosis." Gouguenheim, Lebert, Church, Bartholow, Ponfick, Peacock, Eppinger, Newton Pitt, Gowers, von Hoffmann, Simmonds and others have in later essays, some of which are classic, further widened our knowledge of intracranial aneurysms. In 1907 Beadles was able to report 555 cases, where intracranial aneurysms were found post-mortem, including 114 cases not published before; he too regarded it as quite impossible to diagnose an intracranial aneurysm, except in very rare cases: "I will go further and say that, in the vast majority of cases of aneurysms, tumour even cannot be diagnosed." Wichern (1911) was the first who emphasized the possibility of diagnosing this disease, because fifteen of his twenty-two cases in one way or another had symptoms of previous bleeding before the fatal one. Owing to the position which lumbar puncture had acquired in the preceding dozen years in the neurological clinic, where it was used as a common method of examination, a knowledge of the symptoms of subarachnoid hæmorrhage was established, especially its frequency (G. E. Schroeder), and it became possible to diagnose a ruptured or bleeding aneurysm. Later works of

Fearnsides (1916), Symonds (1923), Borchardt (1925), Parker (1926), and others gave a clearer basis for this diagnosis, particularly as it was shown how often an aneurysm gives rise to hæmorrhage, often several times, before the fatal severe bleeding takes place; a fact which corresponded well with the intermittent picture of the disease. Meanwhile it must be said to be still difficult to distinguish the bleeding of an intracranial aneurysm from other forms of subarachnoid hæmorrhage.

Frequency, Age Incidence and Position.

Before discussing the clinical picture of the disease in more detail, it is necessary to mention the frequency of cerebral aneurysms, their localization, and their relationship to age. Seeing that the smaller aneurysms are frequently overlooked at the post-mortem, it is by no means an uncommon disease. The frequency is diversely stated because of differences in material and technique of examination. The more minute the examination of the arteries of the brain the smaller the aneurysms one will be able to find, and aneurysms which have caused no symptoms during life will more frequently be an accidental discovery at autopsy.

They appear in about one-half to one, or one and a half per cent. of all post-mortems, though sometimes the frequency is stated to be less. Fearnsides found (in 1916) 44 cases out of 5,432 autopsies in all; Osler had previously found aneurysms in 12 cases out of 800 autopsies (cited by Fernsides). Newton Pitt had in the years 1869-1889 only found 23 cases out of 9,000 autopsies. On going through the records of 6,232 autopsies in which intracranial aneurysms were not suspected, Conway found this disease described in 43 cases. Busse had meanwhile by careful examination found in not less than 39 cases out of about 400 autopsies, aneurysmal formations on the anterior communicating artery. According to the statements of Bradford and Turnbull aneurysms are more frequent on the arteries of the brain than on those of the body, whereas the statistics of Crisp (cited by Osler) only show 7 intracranial aneurysms out of 501 cases of aneurysm, whereof 137 were on the popliteal artery.

In the above statistics, as in the following, only genuine aneurysms, or evident saccular or spindle-shaped limited dilatations, are included, while wide or doubtful dilatations of an artery are as a rule omitted. In my material only aneurysms from the size of a pea and larger are to be found. Furthermore, the arteriovenous aneurysms on the internal

carotid artery in its course through the cavernous sinus have been omitted, as, because of the characteristic picture of this disease (pulsating exophthalmos) they naturally form an independent clinical entity (a classic work by Slomann and a new one by H. Ehlers on this subject are to be found in Danish literature). Furthermore, the multiple miliary aneurysms on the smallest branches of arteries which Charcot and Bouchard postulated as a frequent cause of cerebral hæmorrhage have been omitted, since their existence and signification are rather disputed, and they do not fall into the category of real aneurysms (Pick).

The true, larger intracranial aneurysms are almost exclusively localized on the greater extracerebral arteries, most of all on the arteries on the base of the brain near, or forming part of, the circle of Willis. Aneurysms are seldom found in the brain substance (but note my Case 17) or on the convexity of the brain (Reinhardt). The frequency with which the different vessels are attacked is rather differently reported, since with small series of cases accidental variations play a part. The place of predilection for an aneurysm is a bifurcation of one of the great arteries, or the place where smaller branches arise (specially the origin of a communicating artery), because these places anatomically represent the most delicate parts of the wall of the artery (Busse). According to Gowers (1893) they are most frequently to be found on the middle cerebral artery and thereafter with decreasing frequency on the basilar artery, the internal carotid artery, the anterior cerebral artery, the posterior communicating artery, the anterior communicating artery, the vertebral artery, the posterior cerebral artery, and the inferior cerebellar artery. Von Hoffmann (1894) stated the order to be: middle cerebral artery, internal carotid artery, anterior communicating artery, basilar artery, vertebral artery, anterior cerebral artery. The frequency of aneurysms on the basilar artery is very variously computed. Lebert regards them as rare, while von Hoffmann finds them rather often. They are frequently found in my material owing perhaps to the fact that it covers an extraordinary large number of cases of arterio-sclerotic aneurysms, as these tend especially to be located on the large vessels, while the embolic ("mycotic aneurysms," Eppinger) are most frequently found in the smaller vessels.

The 23 aneurysms in my material are grouped in the following way: the middle cerebral (the Sylvian fissure artery) 7 cases, the internal carotid 7 cases, the basilar artery 5 cases, the anterior cerebral 2 cases, the posterior communicating artery 2 cases, the ophthalmic 2 cases, the anterior communicating artery 1 case; in total 26 aneurysms in 23

individuals, as in one case 2 aneurysms were found, and in another case 3, in the same patient. In one case multiple dilatations of very arteriosclerotic cerebral arteries were found in the middle line; 8 aneurysms lay on the right side and 13 on the left. Bradford too found aneurysms more frequent on the left side. Wichern found the aneurysms on the middle cerebral artery more often on the left side. Ebert asserts the same with regard to the internal carotid artery and the posterior communicating artery. This has been explained by the fact that the carotid artery on the left side arises directly from the aorta. Yet Kerpola finds the aneurysms most frequently on the right side.

The incidence in the two sexes is also differently stated; according to Lebert women are more frequently the sufferers, but Hoffmann men. In my material are found seventeen women but only six men. The incidence too is differently stated; intracranial aneurysms are especially to be found between 30 and 60 years of age (Lebert, Krey), but they may be found at all ages.

In Wichern's series only seventy-one cases out of seventy-five were under 30, and only four were more than 60 years old; of the thirty-nine cases by Busse ten had not reached 40 years. The cases in my material vary from 11 to 75 years, whereof only three were under 30 years, while ten patients were over 30 and three over 70. In two cases the age is not known. Intracranial aneurysms thus most frequently give symptoms or involve death in the more advanced age periods, but they may occur in younger patients.

The size of the aneurysms vary from those which can just be seen, about the size of a mustard grain, to the size of a fist (Reinhardt), which no doubt is the largest intracranial aneurysm described. While some authors (e.g., Busse) report rather small aneurysms only found by systematic investigation of the arteries, other authors describe aneurysms of a larger size, e.g., when older post-mortem cases are recorded, as in this work. In my series no aneurysm smaller than a pea was included, two were as large as a plum (*vide* fig. 3), while one was of almost the size of a chicken-egg (previously published as a case report by Harald Møller in 1920).

There does not seem to be any connection between the size of the aneurysms and the localization in the different arteries (*vide* table) and it is more the ætiological factor, age and the like, which play their part here. Thus in Fearnsides' series of thirty-four arteriosclerotic aneurysms twelve were of the size of a pea and nine of them even smaller, while only six were over 6 mm. in diameter, the largest 30 mm.;

of thirteen embolic aneurysms three were of the size of a pea and none smaller, the largest was 25 mm. in diameter.

	The middle cerebral artery	The internal carotid artery	The basilar artery	The anterior cerebral artery	The posterior cerebral artery	The ophthalmic artery	The anterior communicating artery	
Size of a pea	2		1	1	1		1	6
Size of a cherry-stone	1							1
Size of a nut kernel		1						1
Size of a hazel-nut		2						2
Size of a cherry		1	1	1				3
Size of a shell-almond			2					2
Size of a walnut	2							2
Size of a plum		1				1		2
Size of a chicken-egg		1						1
Size of an index			1					1
No statement of size	2	1			1	1		5
Total	7	7	5	2	2	2	1	26

The ætiology is rather differently stated. In newer works congenital anomalies, local diseases in the wall of the artery due to septic emboli in ulcerative endocarditis, sepsis, pyæmia, universal diseases of the arteries such as arteriosclerosis, as well as traumata, are regarded as the most essential factors, whilst syphilis is unimportant. This will be dealt with later on. Arterial hypertension often co-operates with other factors in causing the bursting of the aneurysm.

We do not know how long a large aneurysm may exist without giving symptoms, but judging from the aneurysms accidentally found at autopsy, which have not caused marked symptoms, an aneurysm can exist for many years. Cases where an aneurysm has given clinical symptoms during a series of years have also been reported. One case published by Souques had presented symptoms of cerebral tumour for fifty-five years before the patient committed suicide at the age of 65, but this is a rather exceptional case. Among my cases, one (No. 15) had had symptoms for at least thirty-two years and possibly even longer. Only in a few cases is it possible exactly to determine when an aneurysm is formed, and this in fact only in case of the septic-embolic aneurysms (Wichern); in the case of Foster Moore, the aneurysm

seems to have developed in the course of twenty-four hours, as a sudden blindness on the one eye marked the moment at which it damaged the optic nerve. The aneurysm, which came into existence in the course of morbus cordis, was diagnosed during life and proved eight weeks later post mortem.

Symptomatology.

Among the symptoms of intracranial aneurysms one has to distinguish sharply between the symptoms of the original disease such as arteriosclerosis, ulcerative endocarditis, sepsis, pyæmia, &c., and the symptomatology of the aneurysm itself. In regard to the mycotic aneurysms the demonstration of the original disease is of great significance in diagnosis, but in arteriosclerosis the symptoms of this disease will often mask those of the aneurysm and render diagnosis impossible, as in several of my cases. Among the special symptoms of aneurysm one again has to distinguish between: (1) symptoms of increased intracranial tension; (2) local and focal symptoms caused by pressure or destruction of the nerves of the brain or of the brain-tissue or by atrophy of the cranium, &c.; (3) and finally the symptoms of beginning leakage or developed rupture, i.e., subarachnoid hæmorrhage. Further, a single symptom (intracranial bruit) has been considered as specific for aneurysm.

Symptoms of intracranial hypertension are seldom found in cases of aneurysm. Even in the case of Reinhardt where an aneurysm as big as a fist had caused considerable destruction of the bones of the cranium, there were no symptoms. In septic and syphilitic aneurysms it is very difficult to exclude meningitis as the cause of such intracranial hypertension. Fearnsides did not in any of his other cases find any symptom of this. In the very rare cases of optic neuritis due to aneurysms which are found in the literature, the cause was generally direct pressure of an aneurysm in the neighbourhood of the chiasma on one or both optic nerves and the consequent circulatory disturbances. In cases of bleeding from aneurysms symptoms of intracranial hypertension are very common, e.g., choked discs, although bleedings into the retinal tissue or the optic discs are often to be found and are rather characteristic. The cause is direct pressure on the optic nerve, perhaps from a clot, with impaired outlet from the central retinal vein (Goulden and Riddoch), or infiltration of blood down the sheath of the nerve (Dupuy-Dutemps). A frequent and characteristic symptom is headache, often severe and on the same side; it is as a rule caused by an incipient rupture.

The slow rate of growth and the very soft and yielding nature of

aneurysms explain the above facts, and also the rarity of focal and local symptoms. It is not rare to find, for example, the optic nerve pushed forward and flattened, even imbedded in the wall of the aneurysm, without perceptible reduction of sight (as in my Case 9). Beadles found in only sixteen, or 4 per cent., of his aneurysms any sign of tumour, and in twenty, or 7 per cent., symptoms which might suggest cerebral growths. These local symptoms largely depend on the position, size, quality (calcified or not), rate of growth, &c., of the aneurysm.

The clinical picture depends on the localization of the aneurysms, but common to all is the fact that they sooner or later cause a subarachnoid hæmorrhage. Repeated bleedings often occur at intervals of years, up to 20 years according to Fearnsides. Wichern found this in fifteen out of twenty-two cases, and Fearnsides in about 42 per cent. of his non-embolic aneurysms, but at the same time no less than ten out of forty-four patients were admitted with symptoms of bleeding which soon led to death, without there having previously been evidences of hæmorrhage.

Some authors (e.g., Borchardt) consider every subarachnoid hæmorrhage for which no other cause can be shown as due to bleeding from an aneurysm, at least if the symptoms are intermittent, or if earlier bleedings had occurred. Others, as Guillain, do not mention intracranial aneurysms as causing subarachnoid hæmorrhage. Comte on the other hand gives an instructive description of the pathology and symptoms of intracranial aneurysms.

If we exclude traumatic hæmorrhages in which the nature and force of the injury will always be the decisive factor, it is the symptomatic and so-called "spontaneous" subarachnoid hæmorrhages which are difficult to separate from aneurysmal bleedings. In several cases the subarachnoid hæmorrhage may be idiopathic, but certain forms of hæmorrhagic encephalitis or certain cases of epidemic encephalitis may, apart from the subarachnoid hæmorrhage, pass without symptoms, or with symptoms so "masked" that the diagnosis of the original disease is impossible.

It seems probable that a spontaneous subarachnoid hæmorrhage is in the great majority of cases caused by aneurysm. The investigations of Busse have shown that even small aneurysms may cause a fatal hæmorrhage, that small aneurysms are far more frequent than previously supposed (about 10 per cent. of autopsies) and that these aneurysms are only found by very careful investigation. Gull pointed out in 1859 how difficult it is, post-mortem, to find the aneurysm in a case of

bleeding, where it is quite imbedded in blood-clot. As the examinations of Busse only comprise the anterior communicating artery, aneurysms may be supposed to occur even oftener than stated by him, as the largest aneurysms, even the congenital, are not often found in this situation.

There is, however, an essential difference between aneurysmal bleeding and the other forms of subarachnoid hæmorrhage in that the latter are often (or always?) of venous origin (S. Goldflam), originating from the pial veins or plexus, while bleeding from aneurysms is an arterial bleeding, though often somewhat modified by thrombosis within the aneurysm (Emil John). When rupture threatens, a new coagulum may be formed and the picture of the disease takes an intermittent course, which should make it easier to diagnose. Although other forms of subarachnoid hæmorrhage may occur several times in the same person (Babinski and Jumentié) this is exceptional.

I am, therefore, inclined to suppose that by far the majority of and perhaps all the spontaneous subarachnoid hæmorrhages which result in death are due to aneurysms. I assume that bleeding during several days and nights with remittent symptoms is characteristic, although more rapid courses or even with sudden death may occur. Subarachnoid hæmorrhage occurring several times in the same person, or of a remittent type, is most probably due to an aneurysm. That the post-mortem performed in the ordinary way does not prove this does not exclude the presence of aneurysm.

When a young, previously healthy person is suddenly seized by symptoms of a subarachnoid hæmorrhage and no organic disease of the brain nor a considerable trauma can be shown to be its cause, one must always think of a burst aneurysm. The following cases are cited as examples of this:—

Case 1.—An unmarried woman, aged 23, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, December 18, 1920, and died here December 21, 1920. She was always of a somewhat slender build, of delicate health, sickly, often tired; has had "anæmia," no inflammation of the lungs, no scrofula.

She was taken suddenly ill on December 13, and began to cry aloud on account of violent headache; she vomited the whole first night, not later. She was somewhat confused, remained in bed, took very little food. There was no convulsion or paralysis, but a fixed upward position of the eyes. No grinding of the teeth, stiffness of the neck, nor cry was noted. She dozed, spoke only a few words and complained of headache. Incontinence of urine occurred during the last day and night.

During her stay here she was drowsy, slow, far-off and distracted, but conscious and knew where she was.

On examination.—She was of slender build. Stiffness of the neck and Kernig's sign were present, but no strabismus. The pupils were small and reacted. Knee-jerk, Achilles tendon and plantar reflexes were absent on both sides. Otherwise no neurological signs were noted. Rectal temperature was 38·5° C. on admission, and next morning 38·9° C. Pulse 76 and 80.

December 20, temperature 39·5 to 39·3° C., pulse 84 to 88. There was increasing drowsiness, possibly double vision and facial paresis on the right side, with stiffness of the neck and Kernig's sign. The tendon reflexes in the upper extremities were brisk but were absent in the lower extremities.

On ophthalmoscopic examination, optic neuritis was found in both eyes and in the left eye hæmorrhages near the disc.

Lumbar puncture gave a light yellow, blood-stained fluid which contained twenty-eight lymphocytes and larger mononuclear cells and about 300 red cells per cubic millimetre; globulin was absent, albumin 10 (Bisgaard). No bacilli were found and no growth was obtained on ascites-agar and bouillon.

On December 20 there was no definite paresis of the cranial nerves, but slight outward deviation of the right eye. Temperature unaltered, 39·7° C. Pulse 120.

On December 21 both optic discs were swollen, with exudates and hæmorrhages (optic neuritis). The condition otherwise was the same. She dozed, did not eat and died quietly with increasing hyperthermia.

Clinical diagnosis: Meningitis tubercolosa?

December 22 autopsy: On removing the brain abundant blood streamed out from the underside of the frontal lobe, where many clots were found. The blood came from a cavity the size of a plum in the lower side of this part the brain. In the middle line of the coagulum and to the left of it an aneurysm the size of a cherry was found on the anterior cerebral artery.

The brain was preserved and on section the hæmorrhage was shown to be situated between the brain and the pia mater, but it did not extend into the brain-tissue itself.

The post-mortem also revealed fibrous myocarditis and broncho-pneumonia in the right lower lobe.

The aneurysm was thought to be congenital (further details on p. 526).

The clinical picture of this case did not indicate more than the probability of an aneurysm.

The symptoms of such an aneurysmal bleeding are those of the subarachnoid hæmorrhage. The intense headache is very characteristic; it is violent, as a rule on both sides, at times of neuralgic form (trigeminal irritation), or accompanied by vomiting, dizziness or other cerebral (cortical) symptoms; the irritative symptoms as a rule obscure the inhibitory. Different clinical pictures include convulsive,

hemiplegic, aphasic, meningeal, comatose or purely psychotic forms with mental confusion or hallucinations (Flatau).

The onset may be apoplectiform or more insidious. Before the final rupture sets in there may be symptoms of a menacing rupture, as in the following case :—

Case 2.—A man, aged 26, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital on December 29, 1916, and died within twenty-four hours.

It was learned that his family history was negative. From the information obtained from his fiancée, he had previously been healthy up to the last two or three weeks before admission. He then took to bed with violent pains in the extremities and a very severe constant headache with occasional exacerbations, associated with violent vomiting. There was no fever or disturbance of vision. He had not complained of dizziness before the morning of admission when he was getting up. At 2 p.m. he had an attack of convulsions in all limbs with biting of the tongue, but without incontinence. Since then he had been comatose, but at 3 p.m. he had another similar attack.

He was admitted here half an hour later, totally comatose and very exhausted. The respiration was deep and snoring, about 12 per minute, pulse 62, irregular and soft; rectal temperature 36·6° C. He did not move the right extremities, which were more flaccid than the left and showed increased tendon reflexes. A typical Babinski response was present on both sides. The pupils were slightly contracted, equal, and did not react. No strabismus or ptosis. The right corneal reflex was absent. The right angle of the mouth drooped. He incessantly ground his teeth. The tongue was bitten in several places. The chest was healthy, the heart sounds distant and low, with a somewhat irregular faint systolic murmur, which seemed to be loudest at the apex and at the pulmonary area. No dullness over the manubrium sterni was found. The abdominal reflexes were absent on the right side. Stiffness of the neck and Kernig's sign were not observed. The ears were normal. The ophthalmoscopic examination showed normal conditions, at least in the right eye.

The urine obtained by catheter contained albumin and sugar. A lumbar puncture gave bloody spinal fluid which ran out slowly. The Wassermann reaction of both blood and spinal fluid was negative.

He became feeble, flaccid and pale; the left pupil was larger than the right and neither reacted to light. He died suddenly two and a half hours after admission.

Clinical diagnosis : Subarachnoid and cerebral hæmorrhage; glycosuria.

Post-mortem : A large hæmorrhage in the third ventricle passing down into the fourth ventricle and the central canal was revealed; it originated from an aneurysm at the base of the right temporal lobe arising from the middle cerebral artery.

Except for a traction diverticulum in the œsophagus about 1 cm. deep, nothing abnormal, and especially no evidence of syphilis, was found.

The aneurysm was supposed to be congenital.

This case seems to be so typical that it undoubtedly could have been diagnosed. The picture of the impending rupture was especially characteristic and well pronounced. With reference to the differential diagnosis it should be remembered that a severe degree of albuminuria occurs in subarachnoid hæmorrhage (G. Guillain, Cl. Vincent, Schneider, Symonds) but quickly disappears. Guillain considers a pronounced transitory albuminuria indicative of subarachnoid hæmorrhage, whereas slight albuminuria has no significance. It is probably due to central vasomotor disturbances. In my material the albuminuria was never intense, but transitory albuminuria occurred. The glycosuria, which is frequently seen, is supposed to be of central origin also. Guillain also considers a bilateral Babinski reflex as of certain significance in the diagnosis of subarachnoid hæmorrhage.

When the onset is apoplectiform the differential diagnosis will always be difficult as against a cerebral hæmorrhage, which secondarily bleeds into the subdural space or breaks into the ventricles. There is the added difficulty that a hemiplegia frequently occurs with these forms of subarachnoid hæmorrhage. If the hemiplegia proves to be severe and permanent, or if there is pronounced retraction of the head and deviation of the eyes, then a deeper injury of the brain is more probable (Guillain), but this also may be due to a ruptured aneurysm, as in the second of the two following cases.

Case 3.—A married workman, aged 70, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, May 3, 1921, and died here May 5, 1921.

He had previously enjoyed good health and had never had similar attacks before. He had never been absent from his work during more than thirty years. He is said to have been injured immediately before his admission by falling over a rail; he fell flat on his face and immediately lost consciousness; according to an eye witness he walked with a reeling gait before he fell, then he stood still, swayed a moment and fell. After that he began vomiting.

On his admission to the hospital there was a hemiparesis on the right side with drooping of the right angle of the mouth. Next day he was in a state of coma and did not react; there seemed to be paresis of the right arm, but otherwise no focal symptoms. Babinski's sign was absent; the blood-pressure was 145 mm. Hg. The urine contained sugar. He died in a state of coma, without having regained consciousness, on the afternoon of May 5.

Clinical diagnosis: Hæmorrhagia (?) cerebri. Hemiplegia dextra.

Post-mortem: No fracture of the cranium was found, but very considerable subpial bleeding. This originated from a ruptured aneurysm, the size of a cherry, on the posterior wall of the left carotid artery, at the origin of the middle cerebral artery. The blood had reached both the Sylvian fissures, and the left Sylvian fissure especially was distended by blood. There was no bleeding into the brain tissue itself.

There was slight intimal proliferation, but no arteriosclerosis in the branches of the coronary arteries; diffuse intimal proliferation in the aorta, arteriosclerotic plaques in the descending aorta, and some arteriosclerosis in the abdominal aorta were present. Purulent bronchitis and bronchopneumonia were present on both sides as well as hypertrophy of the left ventricle of the heart. The aneurysm is supposed to be arteriosclerotic.

Case 4.—A man, aged 55, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital October 21, 1916, and died on October 22, 1916. He was brought in by ambulance after an attack of unconsciousness which occurred while he was at work. He was found on admission to be comatose and could not be made to react. All the reflexes, including the conjunctival, were abolished. The pupils were much contracted, the heart normal but its action somewhat irregular, the pulse 66, rather weak, the respiration quickened and groaning. Urine: albumin present, no sugar. Temperature 35·8° C. Later some vomiting and œdema of the lungs with blackish foam round the mouth developed. In the evening a Babinski response was obtained from both feet and the tendon reflexes were fairly brisk. Temperature 39·9° C. Next morning he was moribund, temperature 40° C. There was complete atony of all extremities, and the pupils were maximally contracted. He died quietly within twenty-four hours.

Post-mortem: No evidence of fracture of the cranium. Arteriosclerotic changes were seen in the vessels at the base of the brain. The left hemisphere was distended, and here a considerable hæmorrhage was found, which had destroyed the central ganglia and had broken into the ventricles, which it had distended with blood. On the surface of the brain subpial hæmorrhage was seen round the pons, medulla and cerebellum.

In the disintegrated central ganglia on the left side a more compact nodule was found; this turned out to be an aneurysm, the size of a cherry and full of coagula, on a small branch of the middle cerebral artery.

The heart was of normal size without special hypertrophy of the left ventricle; the valves were normal. The coronary arteries were slightly arteriosclerotic, as was also the abdominal aorta. Fatty degeneration of the liver and the remnants of old tuberculous lesions at the apices of both lungs were found, but no other gross changes. The aneurysm is supposed to be arteriosclerotic.

In the first case a lumbar puncture would have revealed the subarachnoid hæmorrhage; the absence of focal symptoms would have

suggested a hæmorrhage from an arteriosclerotic extracerebral artery. In the last case the aneurysm could not be diagnosed.

The senile brain may react even to severe subdural hæmorrhage, as in the case below, in such a way as to give the clinical picture of a senile or arteriosclerotic confusion.

Case 5.—A woman, aged 72, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, March 23, 1922, and died there April 2, 1922.

No information about similar previous attacks or other diseases was available. She was suddenly taken ill six days before admission, while alone at home, and was found six to ten hours later lying dressed on her bed, soiled with urine and fæces (unconscious?) She had remained in bed since and had been somewhat confused; the last two days and nights she had been very restless, running about on the floor and crying aloud.

When in hospital she was somewhat confused. She did not know where she was and wanted to get out of bed. Temperature 37·8° C. The pulse was 60, regular and strong. The peripheral arteries were rather hard and tortuous, the knee-jerks absent on both sides. On admission the Babinski response was present on the left side, later on both sides. She had to be catheterized. The urine contained albumin (slight). The blood-pressure was 100 to 165 mm. Hg. On March 24 she was more clear and collected, and fairly well oriented; no pareses nor disturbances of speech were noted. The catheter had to be used. On the following days she was rather somnolent. On March 28 she was more tranquil but not quite conscious. On the 29th lumbar puncture gave a diffusely blood-stained fluid, containing 146 cells and about 800 erythrocytes per cubic millimetre; globulin 1, albumin 25. Wassermann reaction was positive in the blood, but negative in the spinal fluid.

Ophthalmoscopic examination showed senile cataract. She was by turns drowsy and very restless during the following days. On April 2, respiration became weaker and she died quietly in the evening.

The clinical diagnosis was encephalomalacia arteriosclerotica, ictus apoplecticus, confusio mentis.

Post-mortem examination: On opening the cranium an enormous hæmorrhage was seen which reached from the chiasma forward along the olfactory tract and round on to the convexity of both frontal lobes. It originated from a small ruptured aneurysm on the anterior communicating artery. In the brain-tissue itself there was no hæmorrhage.

Additional findings were an echinococcus-cyst in the liver, verrucose endocarditis on the valves of the aorta, universal arteriosclerosis and terminal bronchopneumonia. The aneurysm is supposed to be arteriosclerotic.

The motor phenomena may vary greatly. The hæmorrhage may spread along the vessels or under the pia on the cortex, or flat coagula

may form over the hemispheres so that convulsions, perhaps of the Jacksonian type, or hypertonia and spasms of different kinds develop. In four of my cases convulsions occurred. A symptom often found in my cases was abolition of tendon reflexes of the lower extremities. In a few cases this was associated with a bilateral Babinski response. In some cases the increased tendon reflexes of hemiplegia became reduced when a loss of the deep reflexes of both the lower extremities appeared. This loss of tendon reflexes has been described by Guillain among others but is said to be fairly rare. In my material it occurred frequently, at least after the first two days. It may possibly be characteristic of larger (arterial) hæmorrhages. It has been found on several examinations (by different investigators) in most of my patients and must therefore be regarded as certain. It is also extraordinary when compared with the usually increased reflexes of the upper extremities. Sometimes the passage of blood may almost be followed over the surface of the brain and down into the spinal canal. As an example of motor symptoms of irritation the following case can be given.

Case 6.—A woman, age unknown, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, April 30, 1914, and died there May 1, 1914.

She was admitted in a comatose state. No information was available. She moved both her upper extremities occasionally. Slight reflexes were present on both sides. There was some rigidity of the flexors of the elbow joint on both sides, especially the right. The lower extremities were relaxed without reflexes. The pupils did not react to light. The right nasolabial furrow was absent.

A couple of hours later she was still comatose, the arms drawn up and bent at the elbow-joints, the hands clenched and from time to time convulsive movements of them occurred. Leri's reflexes were not present; a Babinski response was obtained on both sides; there was no deviation of eyes or retraction of the head. Cheyne-Stokes' respiration was noted. She died during the night.

Clinical diagnosis: Apoplexia cerebri.

Post-mortem: The surface of the brain was covered all over with coagula, especially round the right temporal lobe and in the anterior part of the longitudinal fissure, round the genu corporis callosi. The arteries were slightly arteriosclerotic. On the left anterior cerebral artery was found a ruptured aneurysm the size of a rather large pea with arteriosclerotic walls. No changes in the bones of the cranium were seen.

The heart was of normal size with normal valves. The coronary arteries

were slightly arteriosclerotic. In the descending aorta arteriosclerotic changes with slight calcification and atheromatous plaques were seen.

The aneurysm is most probably arteriosclerotic, but in the absence of further history the diagnosis was impossible.

A bleeding aneurysm presents the same symptoms as other forms of subarachnoid hæmorrhage; they may be as variable and capricious. The materials for the diagnosis must be gathered from the special course of the hæmorrhage, the way it arises, possibly previous symptoms of impending rupture (headache, vomiting, radiating pains, transient paresis of the cranial nerves) and from the intermittent course of the whole disease. The diagnosis on this basis is far from sure, but a certain presumption is possible that it is a case of aneurysm with hæmorrhage, as in the last of the following three cases, in which the aneurysm was diagnosed during life.

Case 7.—A woman, aged 60, married, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, July 29, 1918, and died on August 10, 1918.

She had been healthy for many years, and there had been no signs of kidney disease. An hour after she had gone to bed in the evening she began to moan in her sleep, was restless, querulous, holding her head. She did not respond when addressed; had "convulsions" during which she fought with both arms and legs, and violent vomiting, and was then admitted to the hospital. Here she was restless, crying "Oh my head," with constant vomiting. Fæces and urine were passed involuntarily; she did not respond when addressed. The right side of the face was smooth and drooping. Later she was stuperose. Next day her condition was unchanged. The pupils were now small and without reaction. Facial palsy was noted on the right side, and plantar reflexes of the Babinski type. The tendon reflexes were absent in both lower limbs. She cleared mentally during the following day, and became more oriented. There was no asymmetry of the face, but a Babinski response was still present on the right side. The urine contained sugar, no albumin. Blood-pressure: 180 mm. Hg systolic. On August 1, the urine contained albumin, no sugar. On August 3, she has conscious and knew where she was. She was allowed out of bed.

On August 4, the temperature was 38·8° C. Objectively nothing abnormal was found. On the following days fever and headache increased. On August 7 she was foolish and confused, with Babinski response on both sides. On August 10, ophthalmoscopic examination of the right eye was impossible, but the left eye showed choked disc. The urine contained albumin. She died the same evening. Lumbar puncture was not performed.

Clinical diagnosis: Coma, glycosuria, subarachnoid hæmorrhage.

Post-mortem: The vessels at the base of the brain were very sclerotic.

The right internal carotid artery was considerably enlarged, and this continued into the right middle cerebral artery, around which there was a considerable hæmorrhage. Similar but less pronounced hæmorrhage was found around the left middle cerebral artery. The hæmorrhage originated from a ruptured aneurysm, corresponding to the right posterior communicating artery, which could not be located. Corresponding to the place of the aneurysm a partly old and a partly new hæmorrhage was found, stretching down around the right optic tract and behind the corpora mammillaria. The subpial hæmorrhage stretched along the vessels right up on to the convexity of the brain.

Throughout the whole aorta very marked arteriosclerosis was seen, with pronounced calcification.

The left ventricle of the heart was hypertrophied. Calcified bronchial glands, a diverticulum of the œsophagus and an ovarian cyst on the left side were also found.

The aneurysm was arteriosclerotic in origin.

Case 8.—A married woman, aged 64, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, December 29, 1926, and died on January 10, 1927.

At her place of work she was said lately to have had attacks of pallor, but they quickly disappeared. Otherwise she was always healthy.

She fell suddenly ill on the day of admission, and her husband found her unconscious on the floor. On admission here she was very restless, wanting to get out of bed, chattering, holding her head. She had obviously totally lost her bearings. She vomited at first and later was nauseated; she made no response when addressed. Objectively nothing abnormal was found. Blood-pressure 160/85 mm. Hg. The urine contained albumin (Esbach 1·5 per cent.).

She regained consciousness the next day, was more collected and was able to give some information, otherwise soporous. The following day she was fairly conscious, quiet, complaining of headache and some nausea. The left pupil was somewhat larger than the right. There was paralysis of the right sixth nerve, but no diplopia. Otherwise no neurological abnormalities and no Babinski response were noted. Lumbar puncture gave blood-stained spinal fluid. Pressure before the evacuation 180 mm. After the evacuation of $1\frac{1}{4}$ cm. 520 mm. (?). On centrifugalizing the fluid was obviously yellowish, containing albumin 60, globulin 3, i.e., increase of albumin beyond the admixture of blood.

January 3. Ophthalmoscopic examination: maculæ and corneæ normal. Myopia progressiva. Choroidoretinitis.

January 5. No complaints, psychically normal. Paralysis of the sixth nerve diminishing.

January 10. In the morning she suddenly collapsed when dressing, and death occurred shortly after.

Clinical diagnosis: Subarachnoid hæmorrhage.

Post-mortem : Very considerable subarachnoid hæmorrhage especially round the pons and medulla oblongata. On the posterior communicating artery an arterial distension rather larger than the size of a pea was found filled with coagula.

The heart showed some hypertrophy of the left ventricle, and the whole heart was somewhat enlarged. The coronary arteries were rigid and tortuous with atheromatous thickenings. The aorta showed rather pronounced sclerotic changes from the arch downwards. Very broad atheromatous thickenings were present in the arch and, to a less degree, in the ascending aorta.

Further findings were myofibrosis cordis, stasis hepatis et renum, fibromata uteri and pelveo-peritonitis chronica.

Microscopic examination of the aneurysm showed no definite inflammatory changes in the wall, but at the point of its origin the intima was thickened. The wall of the aneurysm consisted only of intima and a thin adventitia.

In another preparation a small vessel was seen with thickening of the intima, as well as arteritis of the media and adventitia. Infiltration of round cells was also seen at several places in the medulla oblongata and meninges round the cerebellum. There was extravasation of blood in and round the meninges.

It is likely that the aneurysm was of infectious origin, but its real nature could not be decided.

Case 9.—A widow, aged 49, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, September 19, 1929, and died there September 28, 1929.

In the family of the father there were some cases of apoplexy. Except for otitis media as a child, with resultant deafness of the right ear, and uncomplicated diphtheria in her 28th year, she had always been healthy. The climacteric had begun, but menstruation had not yet altogether stopped.

She was brought to the hospital by the ambulance, having been immediately before found lying unconscious on the floor of the bathroom, where she was taking a warm bath. She had been all right before the bath. She did not respond when addressed, but responded briskly to the examination and to pricks with needles : she was restless, turning about in the bed, and preferred to rest on the left side. There was less movement of the extremities on the right side, at least of the right arm. They did, however, move actively in response to pricks. Tonus and reflexes were normal. A doubtful Babinski response was obtained on the right side. Both eyes were tightly closed ; the right could be opened passively, the left not. The pupils reacted normally. The eyes were moved freely. The right angle of the mouth was slightly smoothed out.

Heart : Limits normal, no murmurs. The action very irregular with extrasystoles. Heart-beats 116, pulse 100. Blood-pressure 180/90 mm. Hg. No meningeal symptoms. The urine contained no pathological elements.

Next day her state was unaltered; she was restless, talking nonsense, confused, and did not know where she was. On sitting up in bed in the morning she suddenly fell back with rattling respiration, became quite pale, and passed urine involuntarily.

September 21. Still somewhat absent and slow, talking nonsense. No aphasia. No paralysis, eyes normal. Knee-jerk and Achilles-tendon reflexes weak, especially on the left side. Plantar reflexes absolutely normal. No meningeal symptoms.

September 22. Temperature yesterday evening 38·5° C., this morning 37·6° C. Tired and somewhat distraught, otherwise physically normal. Nothing was found which might explain the rise of temperature.

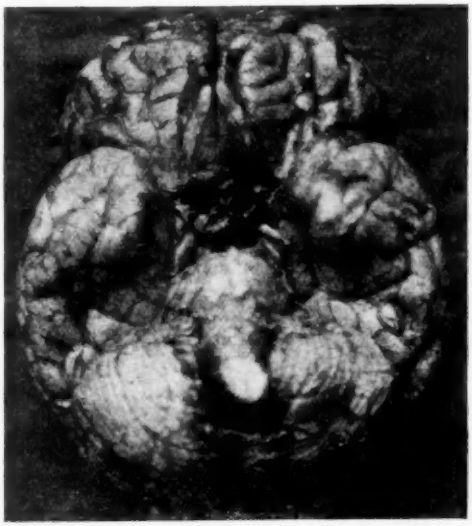

FIG. 1 (*Case* 9).—A ruptured aneurysm on the internal carotid artery in a woman 49 years of age.

September 23. 39° C. to 29·7° C. Yesterday afternoon there was severe headache. She was complaining, dozing or unconscious and had some stiffness of the neck.

Lumbar puncture: Spinal fluid blood-stained, identical in three portions. On centrifugalizing the fluid on top is slightly yellowish. It contains 31 cells and 13,000 erythrocytes. Globulin 1? albumin 14.[1] Probably slight increase

[1] Determined by the methods of Brandberg, Stolnikow, Ross, Jones and Bisgaard. In this paper, globulin refers to that part of the protein content of the spinal fluid which is precipitated by semi-saturation with ammonium sulphate. Albumin is the portion of protein which is precipitated by nitric acid as in Heller's test.

of cells, no evident increase of albumin more than due to the admixture of blood. The Wassermann, Sigma and Kahn reactions of the blood and cerebrospinal fluid were negative.

September 24. Increasing meningeal symptoms. Ophthalmoscopic examination · a couple of small hæmorrhages on the right optic disc and around the disc, otherwise normal.

Increasing meningeal symptoms and stupor.

September 26. Hemiplegia of the right side with motor aphasia. Right plantar reflex absent, left normal. Fixed position of the eyes upwards and to the left. Slight twitching in the muscles on left side. The patient died with increasing meningeal symptoms on September 28.

Clinical diagnosis: Aneurysma cerebri rupta.

Post-mortem: On removing the brain, a small amount of blood was found in the anterior fossa in the subdural space, together with some subpial hæmorrhage in front on the surface of the right frontal lobe, and a smaller compact hæmorrhage on the lower side of the cerebellum. The leptomeninges were hyperæmic. On the left internal carotid artery a thin-walled aneurysm, scarcely the size of a hazel-nut, was found; it compressed the left optic nerve, which was stretched over its anterior end. The aneurysm seemed to originate from the main stem, not from the communicating artery. It did not seem to be in connection with the cavernous sinus. It was not possible to determine the exact place of the rupture, but a small piece of the base of the aneurysm remained behind on the lateral edge of the sella when the brain was removed. On horizontal section through the brain, hæmorrhage was found in both the lateral ventricles. No signs of external violence of the cranium, and no signs of fracture were present.

The heart was normal, the coronary arteries slightly sclerotic, the aorta without dilatations and only slight atheromatous changes. Otherwise nothing abnormal, excepting hypostasis in both lungs, was discovered.

The microscopical examination of the aneurysm showed considerable thickening of the intima with atheromatous degeneration, and in several places layers of calcium. The media was thin, the elastica interna frayed.

Histological diagnosis: Aneurysm with atherosclerosis.

These three cases give rather characteristic pictures. The two first should at any rate have suggested a burst aneurysm, especially Case 8, in which the paralysis of the abducens pointed in the direction of an aneurysm on the posterior communicating artery. The fact that the diagnosis was considered possible in the last case is due to the characteristic cause of the bleeding (congestion by the warm bath) and the intermittent course of the disease. In Cases 7 and 9 the increase in the temperature was the first sign of a renewed bleeding, as it sometimes is (Zádor).

On the whole a rise of temperature is not rare, especially in more

chronic cases; it is due either to direct central irritation or to absorption of the hæmorrhage. If such an increase of the temperature occurs together with torpor or stupor, and if the aneurysm at the same time causes paralysis of the ocular muscles (e.g., aneurysms on the posterior communicating artery) the differential diagnosis as against encephalitis is difficult, especially since one may, despite a large subarachnoid hæmorrhage, occasionally obtain normal spinal fluid by lumbar puncture. (Pierre Marie and Faure-Beaulieu, Barth and Cahen, Zádor.)

In twenty of my twenty-three cases aneurysms have been the cause of hæmorrhage and this hæmorrhage has been the direct cause of death. In some cases death occurred quickly; thus two persons died immediately on their arrival at the casualty room of the hospital (in one case there were, however, other causes of death), in other cases not until hours later or even after several days. How frequently hæmorrhages previous to the one which led to admission had occurred is not indicated in my material, as the histories are not exhaustive in all the cases. The process and symptomatology of this hæmorrhage have been illustrated by different examples. In the following case hæmorrhage occurred in association with acute miliary tuberculosis; unfortunately both the history of the disease and the objective examination of the patient are missing in this case.

Case 10.—A girl, aged 11, was admitted to the Department for Nervous and Mental Disease of the Kommunehospital, March 29, 1914, after four hours of convulsions at home and died on her arrival.

Post-mortem: The dura was slightly adherent to the pia. There was considerable hyperæmia of the vessels and numerous subpial hæmorrhages on the convexity of the brain as well as on the foremost part of the base round the chiasma, on the lower side of the frontal lobes and in the Sylvian fissure, where the tissue was diffusely infiltrated with blood. No tubercles or gelatinous exudates could be seen. At the entry to the left Sylvian fissure, just where the left Sylvian artery arises, an aneurysm the size of a pea was seen.

Microscopic examination showed a simple rupture of an aneurysm without cellular infiltration of its wall.

The middle lobe of the right lung consisted entirely of a system of bronchiectatic cavities. Both lungs and the spleen were sprinkled with miliary tubercles. The upper mediastinal glands were caseous, otherwise nothing abnormal was found.

The aneurysm must be regarded as congenital.

A more detailed pathogenetic explanation of this case is scarcely possible; it is uncertain whether the aneurysm might have been

diagnosed at an earlier date. In cases of coincidence between an aneurysm and other intracranial disease the diagnosis of the aneurysm will as a rule have to be excluded beforehand. In two cases an aneurysm, which had not ruptured, was found as an accidental post-mortem finding in cases of organic encephalopathies.

The first case was an old woman, aged 64 (Case 11), who had a soft (arteriosclerotic?) aneurysm, scarcely the size of a plum, on the left ophthalmic artery just before it passed through the foramen opticum. The aneurysm extended in a dorsomedial direction, was firmly adherent to the optic nerve, which it compressed, and had caused a depression, the size of a walnut, in the trigonum olfactorium. There was also an encephalomalacia, the size of a rather big nut, in the left lenticular nucleus, in addition to a smaller one high in the left frontal lobe. The Wassermann reaction in the spinal fluid was positive and there was a strongly positive reaction in blood. The history indicated two confusional states with aphasia and right hemiplegia occurring at intervals of months.

In the other case, that of an old man, aged 75 (Case 12), with senile arteriosclerotic confusion and dementia, an aneurysm about 2 by 1½ cm. in size and filled by clots was found on the basilar artery (fig. 6). Under the left temporal lobe a psammoma, about 1 cm. in size, was found and in the cerebellum a fairly large softening.

In a third case, a man aged 49 (Case 13), with encephalopathia luetica, a spindle-shaped dilatation, the size of a forefinger, was found on the basilar artery (*vide* fig. 2).

Case 13.—A married man, aged 49, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, April 21, 1921, and died on June 5, 1921.

The father's brother died mentally ill.

About twenty-six years ago he was treated here at the hospital for mental depression. He had lues twenty-one years ago, and was treated four times with inunctions and injections, but never with salvarsan. He had had no later symptoms.

From November 7 to 13, 1916, he was treated in the Department for Mental and Nervous Diseases of the Kommunehospital under the diagnosis dementia paralytica. At that time he had already for several years suffered from "nervousness," exhaustion and rheumatoid pains in the loins and back, and in the knees, but never real lancinating pains. His state of mind was one of depression. He complained of pain in the precordia. Objectively no positive signs of dementia paralytica were found. Heart: accentuated second sound, otherwise normal. Pulse 78, somewhat high tension. Skin

reflexes weak, plantar reflexes not obtained. Knee-jerk and Achilles-tendon reflexes absent. No ataxia. Otherwise no neurological abnormalities. Lumbar puncture: cells 16 with 70 red cells, albumin 40, globulin 3, Wassermann reaction in fluid positive, in serum negative. Urine normal.

His condition had later gradually grown worse, especially during the time previous to his admission. He complained of continual low spirits, irritability, bad temper and increasing loss of memory. Of late there had been a fair amount of headache, a few attacks of vomiting and periodic dizziness. From time to time he had diplopia, and rheumatic pains in the extremities, but no lancinating pains, no girdle feeling or gastric crises. His urine sometimes passed involuntarily. His gait became increasingly unsafe, especially in darkness; he had sometimes fallen and had had difficulty in getting up again. During his stay at the Department he was rather dull; it was difficult to make him adjust himself to the rules of the hospital and to respect decorum. His spontaneous speech showed some hesitation, the test words were repeated fairly well, but there was definite impairment of perception.

He was much aged and with a dull appearance: there was slight ptosis of the eyelids, the pupils were equal and did not react to light. From time to time there was fibrillation of the muscles of the face. The abdominal reflexes were present. Extremities: Some power retained, no ataxia, the tendon reflexes were lively in the upper extremities, the knee-jerks and Achilles-tendon reflexes were not obtained, even when the patient was placed on his side. No loss of sensory functions. The senses of stereognosis, locality and position were retained; he walked with a broad base, slightly tottering; Romberg's sign positive. Slight ataxia to knee-heel and finger-finger tests. Pulse regular, tense. The blood-pressure was over 240 mm. systolic. The urine did not contain pathological elements.

April 23. Lumbar puncture: fluid clear, $3\frac{1}{2}$ cells, 5 globulin, 25 albumin, Wassermann reaction in fluid positive, in serum negative.

April 23. Babinski response definite on the right side.

April 24. Examination of the eyes: Visual acuity, L. $\frac{5}{12}$, R. $\frac{5}{12}$. The patient from time to time mentioned double vision corresponding to a slight paresis of the left external rectus muscle, but after having looked at the object for some time the pictures came together. On the whole the range of all movements seemed to be diminished. The left pupil was a little larger than the right, reacted to light and well on accommodation, but defectively on convergence. Ophthalmoscopic examination and the fields of vision were normal.

He was given antisyphilitic treatment with injections of calomel and neosalvarsan.

June 4. Suddenly yesterday evening he vomited and became weak on the left side. Since then he has been flaccid, with upward-turned eyes and snoring respiration. He vomited continually and became stuporous, more restless and incontinent. The hemiparesis remained unchanged and he died next day with a moderate increase in the temperature.

Clinical diagnosis: Encephalopathia luetica (dementia paralytica?). Hæmorrhagia cerebri.

Post-mortem: On the base of the brain, especially in the cerebello-pontine angle, a hæmatomata the size of a child's hand was found, originating from an aneurysm of almost the size of a fore-finger, on the basilar artery.

The vessels of the brain were very sclerotic (fig. 2).

The heart was somewhat enlarged, the left ventricle hypertrophied. Nothing abnormal was seen on the valves, but in the descending aorta typical plate-like thickenings in the media were found, with wrinkling of the intima, and what

FIG. 2 (*Case* 13).—Spindle-shaped aneurysm in a man 49 years of age who suffered with endarteritis obliterans.

was undoubtedly an aneurysm. The coronary arteries were rather stiff and calcified, and in the myocardium coarse patches of fibrous tissue were found.

The kidneys were rather small, but of equal size. The capsule was easily removed, the surface rather granular; the cortex was narrow, the kidney structure obscured and the vessels distended.

The microscopic examination of different parts of the brain cortex, brain stem, cerebellum, medulla oblongata and spinal cord showed widespread arteritis obliterans of the smaller and medium-sized vessels and some perivascular infiltration with round cells, but no changes typical of dementia paralytica.

The microscopic examination of the aneurysm is described later (p. 528).

Although the symptoms of hæmorrhage in the last case were rather characteristic, it was, as in the two other cases, impossible to diagnose during life.

It will be evident from what has been stated that in hæmorrhage from an intracranial aneurysm there is no pathognomonic symptom by which an aneurysm may be diagnosed. But the course of the hæmorrhage may suggest in some cases (and more frequently than has hitherto been the case) that it originated from an aneurysm, especially when there are symptoms of impending rupture. If before the hæmorrhage there had been local or focal symptoms the diagnosis may be made with reasonable certainty.

On the other hand, when the aneurysm has not given rise to hæmorrhage it is very important to make the right diagnosis on the local symptoms from the point of view of treatment; partly because in most cases an operation carried out on the diagnosis of tumor cerebri would be fatal on account of the hæmorrhage, partly because of the possibility of a rational treatment of the aneurysm if the diagnosis is made in due time. In some cases the clinical picture is so characteristic that it is possible to make a diagnosis. In the cases of Beadles the aneurysms on the basilar artery gave symptoms before the bleeding began in 50 per cent. of the cases: those on the posterior communicating artery in 47 per cent.; those on the posterior cerebral artery in 41 per cent.; while aneurysms on the middle cerebral artery produced symptoms in 22 per cent. only. Aneurysms on the internal carotid artery in its course through the sinus cavernosus caused symptoms in 69 per cent., those in the rest of its intracranial course only in 31 per cent.

The aneurysms on the basilar artery are thus those which most frequently cause symptoms (excluding the intrasinus aneurysms on the internal carotid artery), and the most characteristic clinical picture; if the latter is not clear cut, the diagnosis is difficult. Krabbe and Backer (1922) collected cases of the latter type from the literature, and have at the same time reported one new case and sketched the clinical picture. The most characteristic symptom is the appearance of temporary slight hemiplegia alternately on the two sides, the consequence of pressure first on one, then on the other pyramidal tract (Carl Lange, 1872). In addition to pyramidal symptoms and possibly sensory disturbances, paralysis of different cranial nerves, depending on the site of the aneurysm, may be found, e.g., in the upper part of the basilar artery the oculomotor nerve suffers; aneurysms of its middle and lower parts may affect the trigeminal, abducens, facial, acoustic and even the posterior

cranial nerves. These may be combined in different ways; as a hemiplegia alternans or quadriplegia; one limb may be only slightly paralysed; or there may be deafness, difficulty in speaking, swallowing, or respiration, or radiating pains of different kinds, besides the characteristic headache, which as a rule is localized to the back of the head. Comte rightly emphasizes that the patients as a rule are psychically intact up to the time of death.

Of my five cases one shows such a picture:—

Case 14.—A man, aged 66, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital: (1) January 5 to February 14, 1908, and (2) September 4, 1914, and died there September 7, 1914.

He had been healthy before, apart from a series of traumata, including some of the head, as for example falling from a height of about 40 ft. This was followed by a stay in hospital for seven weeks. There were no paralyses or other sequelæ of the accident. In May, 1907, he began to feel ill with pains in "the throat" on bodily effort. The pain started in his palate and passed through his neck down to his chest. Nine days before admission he had "pneumonia" (?) with very high fever. He had difficulty in speaking during the first days and talked a lot of nonsense. From the beginning of the disease there was severe headache on the right side and severe pains in the right side of his throat, and in his right shoulder and upper arm; on the third day severe vomiting set in. He had also for a couple of weeks had pains "like a wound in the mouth," radiating up to the right orbit. On admission he was highly feverish with herpes labialis. He appeared to be in pain. The expression of the face was somewhat mask-like, the right angle of the mouth slightly drooping and the right nasolabial furrow slightly smoothed, with slight ptosis of the right eye and overaction of the frontal muscle. The right pupil was smaller than the left. The tongue and soft palate were moved naturally. The cranium was rather irregular with a great depression corresponding to the coronal suture. The tendon-reflexes of the lower extremities were absent on both sides. Babinski's sign was absent. The chest did not show anything abnormal.

January 7, 1908. Condition of pupils unchanged. Ptosis evidently diminished. The tendon-reflexes to-day were lively on the left arm and all present, but very slight on the right side, and the muscles were flaccid. He was somewhat uncertain on finger-to-finger test and finger-to-nose test with the right hand. There was slight hyperæsthesia and hyperalgesia on the right side of the forehead, the temple and especially the back of his neck, and also on his shoulder, and diffusely all over the right hand and arm. On the left upper extremity perhaps some hypalgesia and hyperæsthesia. When lying on his side the knee-jerks were very lively, the right ankle-jerk was feeble, the left fairly brisk.

The urine contained no pathological elements. Temperature normal. Examination of throat for diphtheria negative.

On the following days he complained of pains in the right side of the head, especially over the right supra and infra-orbital foramina and in front of the right ear.

January 16. Pains in the face diminished.

January 21. Right pupil is still only the size of a pin, but reacts to light. Knee-jerks now lively, tendon reflexes in both upper extremities lively. No Babinski response. Evident hyperalgesia on right foot and leg. Sense of localization and position a little uncertain on the right foot. On the rest of the right half of the body a tendency towards hyperalgesia.

January 25. No special complaints. The tip of the tongue diverted a little to the right, and the right angle of the mouth drooped. Reflexes present. Hypalgesia on left upper extremity, but no other loss of sensory function.

February 14. Discharged well.

Clinical diagnosis: Influenza with pneumonia.

He had not been well since, but had had pains in both legs, every evening, with pains in the throat and in his right arm. The day before readmission he became more weak, could not stand on his legs, nor had he any strength in his arms; he complained of severe headache, and was drowsy.

On examination he had an aged appearance; the right angle of the mouth drooped. His tongue moved normally. He talked slowly. The pupils were equal, contracted and reacted to light. Reflexes on both upper extremities lively, no clonus. Knee-jerks not obtainable. No loss of sensory functions.

Heart and lungs: emphysema. Heart sounds faint. Only slight peripheral arteriosclerosis. Temperature 38·3° C.

Some hours later he was restless and confused and had difficulty in speaking and in swallowing, but was conscious, explaining himself by means of signs. The left pupil was bigger than the right, both reacting slightly to light. Paralysis on the left side of the face was noted and considerable paralysis of the left leg and of the left arm, with increased tendon-reflexes and obvious Babinski response, together with reduced sensitiveness on the left side. He quickly became weaker, developed Babinski's responses on both sides and Leri's reflexes and died with increasing hyperthermia, but was conscious till the end, on September 7.

Post-mortem: On the base of the pons a considerable dilatation of a very sclerotic basilar artery was seen, which in one place formed an aneurysm twice the size of a nut, with thin, discoloured, translucent walls, filled with fine cobweb-like adhesions. Similar adhesions were found all over the base, forming a net over the fissures and the arteriosclerotic vessels. The brain was not further examined.

In the aorta arteriosclerotic changes were especially pronounced in the arch and in the lowest part of the abdominal aorta. The iliac arteries were almost totally calcified. At one place in the beginning of the thoracic aorta a large whitish cushion-like thickening was found. In the ascending part just above the aortic valves small nodules, cicatrices and an arteriosclerotic

patch, the size of a sixpence, were found. The heart weighed 570 grm. There was considerable hypertrophy of the wall of the left ventricle, not of the right. There was atrophy of the papillary muscles on the posterior valve of the mitral and of those in the right ventricle, and at the apex of the ventricle a parietal thrombus, the size of a rather big nut. The myocardium was abnormally firm with considerable nodular areas of fibrous tissue. The coronary arteries were arteriosclerotic.

The kidneys were atrophied with a greatly narrowed cortical zone, the capsule adherent, the surface finely granulated, the structure well marked. The urinary organs were otherwise normal. Microscopic examination of the aorta revealed pronounced thickenings of the intima and calcification on the border of the media with doubtful inflammatory changes.

The corpse was strongly built, and well nourished; weight $56\frac{1}{2}$ kg.

In this case the local symptoms were characteristic, while on the other hand the symptoms of bleeding were indefinite. But the picture of the disease did at least point in the direction of an aneurysm on the basilar artery. The increase of temperature on admission was probably caused by the hæmorrhage, as in the hospital it was impossible to find anything abnormal in the chest. The adhesions, fine as a veil, all over the base of the brain are, though not common, yet clearly an expression of repeated small bleedings from the aneurysm. Whether the aneurysm in this case was syphilitic, it was not possible to decide. According to Saadhoff, syphilitic aneurysms are mostly found on the basilar artery.

In a previous case (No. 13) the aneurysm on the basilar artery did not give distinct independent symptoms, and on account of the complicating luetic encephalopathia could not be diagnosed. In the third case (No. 12) the aneurysm produced no recognizable symptoms and was unruptured. In the fourth case (No. 10), already mentioned, information was not obtainable, but the combination with miliary tuberculosis excluded, I think, the possibility of diagnosing an aneurysm. In the fifth and last case (No. 16), where, in a 40-year-old woman, a ruptured aneurysm the size of a cherry was found on the basilar artery, no information was available, as the patient was admitted in a state of coma and died soon after.

An aneurysm on the internal carotid artery, which is the most frequent site in my material, also often gives symptoms, especially when situated in the cavernous sinus (in 69 per cent., Beadles). In these cases compression of the nerves which run in the wall of the sinus is found, with paralysis of the eyes, neuralgia of the ophthalmic nerve, and perhaps also compression of the optic nerve. On rupture an

arterio-venous aneurysm with pulsating exophthalmos is formed. Aneurysms in this part of the artery do not occur in my material. Aneurysms on the first intracranial part of the internal carotid artery may also cause characteristic clinical pictures, as shown by Paul Møller amongst others, but the symptoms are far from constant. The most frequent are increasing paralysis of the eye muscles and diminution of vision, perhaps optic atrophy on the same side, accompanied by headache, and later also trigeminal symptoms. Besides total internal and external ophthalmoplegia there may be paralysis of the facial nerve, and these symptoms may be combined in different ways. Such a case is the following (published before by Harald Møller) :—

Case 15.—A woman, aged 53, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, January 1, 1916, and died there January 2, 1916.

From her earliest childhood she suffered much from headache and at any rate for the last thirty-two years had attacks of violent pains in her head, which occurred once or twice in the week; they were unilateral, most violent at the back of her head and in the right side, but also in the left side. Sixteen years ago a decrease of the sight of the right eye was noted; five years later paralysis of the eye muscles and considerable loss of the vision of this eye set in, and nine years ago complete blindness of the right eye and ophthalmoplegia. A year ago spasmodic pains developed in her right eye and around it, and also a typical neuralgia in the first and second branches of the right trigeminal nerve. The pains constantly increased in spite of large doses of morphia. During the last days before admission the pain had been very violent; she became comatose on the day of admission.

On admission she was comatose. The right pupil was dilated, no paralysis of the face, the reflexes in upper extremities were increased, knee-jerks not obtained, from both feet a Babinski response could be elicited.

Post-mortem: On opening the cranium a large hæmorrhage was found, stretching on to the convexity, but it was most pronounced on the base of the brain and especially round the anterior poles of the temporal lobes. In the right middle cranial fossa, near the basi-sphenoid, a thin-walled aneurysm was found, scarcely the size of a chicken-egg, partly filled with coagulated blood. The cavernous sinus was not seen. The right optic nerve was compressed; between the aneurysm and the tip of the petrous bone were found the remains of the Gasserian ganglion. On the internal side of the base of the right temporal lobe there was an impression of the aneurysm.

In the aorta there were diffuse thickenings of the intima; the left ventricle of the heart was hypertrophied, and slight sclerotic changes were found in the coronary arteries. The kidneys showed chronic nephritis.

The aneurysm seems to have been congenital.

The history of her disease does not give any information of a previous rupture, yet the case is so characteristic, not least its protracted course, that a probable diagnosis might have been made. A series of similar cases has been reported from different quarters, amongst others by Taylor Harris and by Conway; in Conway's case there was a paroxysmal increase in the headache on effort (lifting of burdens, &c.). But there is also a series of cases in which the aneurysm has compressed the chiasma and produced a picture similar to that of a tumour of the hypophysis with bitemporal hemianopia leading to optic atrophy on both sides (in the cases of Kümmel even dystrophia adiposo-genitalis).

Case 16.—A woman, aged 40, married, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, January 26, 1919, and died there January 27, 1919.

She was admitted in coma. She was said to have been healthy up to a year ago, when she observed that the vision of her right eye became weaker, and about the same time she got severe headaches, especially localized to the neck. The vision in her right eye diminished, and she became blind in this eye. About three months before admission the vision of the left eye also began to weaken and became very reduced. The headache increased and had been very severe and constantly present. No acromegalic symptoms. Psychically nothing extraordinary.

On the day before her admission she suddenly had an attack of unconsciousness. There were also said to have been convulsions which lasted for several hours in which she bit her tongue and passed fæces involuntarily.

She was admitted in a deeply unconscious state, and did not react when addressed. The right pupil was larger than the left, and did not react at all to light; the left pupil only reacted slightly and slowly. No marks of tongue-bite.

Heart and lungs healthy. Temperature 39°C. Pulse strong and regular 76.

She seemed unable to move her left arm; the triceps reflexes were absent, the ankle-jerks and knee-jerks weak. A trace of Babinski response on both sides. She died within a few hours.

Lumbar puncture and estimation of the blood-pressure not performed.

Clinical diagnosis: Coma, convulsions. (Tumor cerebri?)

Post-mortem, January 28: When the brain was removed a considerable infiltration by blood of the pia mater at the base of the brain was found, reaching forward on the right side over the orbital roof where there were several fairly large flat clots. After removing these a spherical aneurysm was seen, the size of a plum, on the right internal carotid artery, ending exactly at its division and lying on the optic chiasma which was very much compressed by the aneurysm. It had formed a cavity in the brain tissue (in the fossa interpeduncularis) and compressed the stalk of the hypophysis which lay behind it, together with the hindmost part of the olfactory

tract, especially on the right side. The aneurysm, which lay slightly to the right of the middle line, had ruptured on its anterior and inner surface and was partly folded together, but it still contained some fresh coagula. Considerable infiltration of blood was found in the lower medial part of the right frontal lobe, which was softened (fig. 3).

Earlier and more recent tuberculous changes were found in both lungs together with an open foramen ovale in the heart.

The aneurysm was supposed to be congenital.

FIG. 3 (*Case* 16).—A burst aneurysm the size of a plum, on the right internal carotid artery, in a woman 40 years of age.

Before a case such as the above gives symptoms of hæmorrhage, it is almost impossible to make a differential diagnosis from a tumour of the hypophysis. To this must be added that aneurysms on the internal carotid artery not seldom cause destruction of the bones, especially destruction of the sella, which in no way differs from the destruction caused by a tumour of the hypophysis (Albl). In this case the only possibility of making the differential diagnosis occurs when the aneurysm contains so much calcium that it gives a shadow of its own on the skiagram (*vide infra*).

In Case 9 an aneurysm, the size of a hazel-nut, on the internal carotid artery had not given subjective symptoms before the rupture;

even though the optic nerve was found stretched over its front wall, there had been no complaint of defective vision. In the case of a 59-years-old woman with definite lues spinalis (tabes ?) a ruptured aneurysm, the size of a pea, was found on the internal carotid which had not given symptoms apart from the fatal hæmorrhage. One year before, ophthalmoscopic examination had, except for Argyll-Robertson's symptom, shown normal conditions. A fifth case (No. 3) had given no symptoms previously; in the sixth and last case the history and the examination are not complete (the patient died on arrival at the hospital).

Aneurysms on the ophthalmic artery are not likely to give characteristic symptoms. In the case of a 75-years-old woman with syphilis (Wassermann reaction positive in fluid) an aneurysm the size of a plum was found on this artery; two foci of softening on the same side were probably the explanation of the two attacks; that the aneurysm had mechanically caused the latter (or endarteritis obliterans ?) is possible. In cases of aneurysm here, as in the case of those on the anterior communicating and the anterior cerebral arteries, psychical symptoms are said to occur in addition to possible disturbances of vision or anosmia.

The aneurysms on the posterior communicating artery give symptoms related to the oculomotor nerve and the abducens nerve together with disturbances of the trigeminal nerve, and may in certain cases give rather characteristic clinical pictures. In neither of my two cases were symptoms present before the hæmorrhage; in one case (Case 8) after the first hæmorrhage there was a paralysis of the abducens, which might have aided the diagnosis.

Spontaneous subarachnoid hæmorrhage, accompanied by paralysis of the eye muscles, neuralgia in the trigeminal territory or optic atrophy, may on the whole be said to be indicative of the presence of an aneurysm.

Aneurysms on the middle cerebral artery seldom give local symptoms, but may cause convulsions; they are often impossible to diagnose before they burst, as in my Case 4. The convulsions are of epileptiform or Jacksonian type and are followed by transient paralysis, which later may become permanent; sometimes a permanent hemiplegia may develop due to encephalomalacia.

In two of the cases, aneurysms, the size of a pea, on the middle cerebral artery, gave no symptoms at all, neither before nor during the rupture. In a third case an aneurysm on the left side, the size of a walnut, was associated with hemiplegia of the left side and paralysis

of the left oculomotor nerve. This case clearly illustrates the slight importance of the local or focal symptoms in a manifest hæmorrhage; even distant parts of the brain may give symptoms either directly owing to the hæmorrhage or indirectly owing to disturbances of the circulation. Most frequently it is even impossible to determine on which side the hæmorrhage had its origin. Bilateral convulsions were found in one of the cases mentioned, but this has also occurred with a burst aneurysm of the basilar artery. Only in one case, which in many ways is rather exceptional and therefore is reported in detail, did we find distinct focal symptoms which, as the aneurysm had not caused any hæmorrhage, led to the diagnosis of tumor cerebri.

Case 17.—An old woman, aged 66. Twenty years previously she had been infected with lues, and had fifty treatments by injections. Three years later she gave birth to stillborn twins. In May, 1907, she had attacks of unconsciousness with hemiplegia of the right side, for which she was treated at Sundby Hospital until July 14, 1907. During the stay there no signs of syphilis were observed. The paralysis disappeared fairly quickly. In 1918 she was operated on in Bispebjerg Hospital for ventrofixation of the uterus. The Wassermann reaction was not performed; during her stay no signs of syphilis were observed.

During several years she became increasingly confused and vague; she sometimes went out without being dressed, turned on the gas, cut her dress to pieces, &c. She had decreasing power of perception, but good memory for previous events; attacks of unconsciousness became increasingly frequent during the latter years. She suddenly goes red in the face, the eyes turn upwards, she cries out, becomes stiff and later flaccid. She does not remember the attacks, which are of short duration; after many of the attacks there is a temporary asymmetry of the mouth and paresis of the tongue. Later she became more irritable and unsociable and for the last one and a half years uncleanly with incontinence of urine.

When admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, October 4, 1928, she was childish and slightly euphoric, smiling foolishly. There were no speech disturbances of amnestic or dysarthric nature, but she articulated rather badly: on the other hand, from time to time she mistook words. Her power of apprehension was poor, as seen in testing sensation and power of localization.

Ophthalmoscopic examination: The left pupil a little smaller than the right, both react slightly to light and well to convergence. Field of vision and ophthalmoscopy normal except for early cataract of both eyes.

Examination of ears difficult on account of inaccurate statements of the patient, but it seems to show deafness on both sides with pronounced loss to high tones, most in the left ear. This seems to suggest nerve disease and corresponds more to lues cerebri than to a tumour.

There did not seem to be anything wrong with the rest of the cranial nerves, but the tongue deviated a little towards the left, with perhaps fibrillation: the trigeminal nerves were not affected.

Upper extremities. Right: No localized muscular atrophy, but the muscles on the whole rather slack, and their strength poor. Sense of posture and stereognosis present. No ataxia. Tendon-jerks weak. Left: The general condition the same as on the right side, but the muscular strength rather difficult to judge on account of disease of the bone in the left elbow after an old fracture. Perhaps slight paralysis of the left hand, some ataxia or irregularity in the finger-to-nose test; sense of position apparently unaffected, no astereognosis; tendon reflexes weak.

Abdominal reflexes absent, abdomen large and slack. No paralysis of the bladder.

Lower extremities. Right: Muscle strength feeble, slack musculature without localized atrophy. Sense of localization and position as well as superficial and deep sensibility intact; slight irregularity in muscle movements, but no ataxia, tendon reflexes absent. Almost normal plantar reflex. Left: Similar conditions, except that the plantar reflex is sometimes of the Babinski type.

Her walk was feeble and unsteady, only a few steps were possible. It was impossible to test for Rombergism. Examination of sensibility: Brush and pin prick localized rightly everywhere. Perhaps a slight universal hypalgesia, but the statements were unreliable.

A rather obvious senile myxœdema. Spinal fluid clear, colourless, less than one cell, globulin 0 (1?), albumin 26, Wassermann and Sigma reactions in blood and spinal fluid negative, Kahn negative (by sensitized antigen positive).

X-ray: In the right temporal region small calcified shadows are seen, which are probably caused by an intracranial formation in the middle cranial fossa (see fig. 4). The left elbow shows no changes characteristic of syphilis.

During the stay here she had a series of attacks, most often in the night, beginning with a cry, followed by unconsciousness and turning of the head to the left, but no spasms or convulsions. Postparoxysmal paralysis was not seen.

As her attacks were presumed to be connected with a tumour in the right frontal lobe, and the position of the latter seemed superficial, an operation was advised.

This was performed at the Surgical Department of the Kommunehospital under local anæsthesia and slight chloroform-ether inhalation. After the dura mater was split, nothing abnormal was revealed on the surface of the brain, but the tumour was felt on palpation as a hard formation, immediately under the surface. It was enucleated easily and quickly, but was found to stretch rather far into the depth of the hemisphere. Profuse bleeding from the bed of the tumour set in during which the patient collapsed: in spite of repeated tamponades the hæmorrhage continued and the patient died a few hours later.

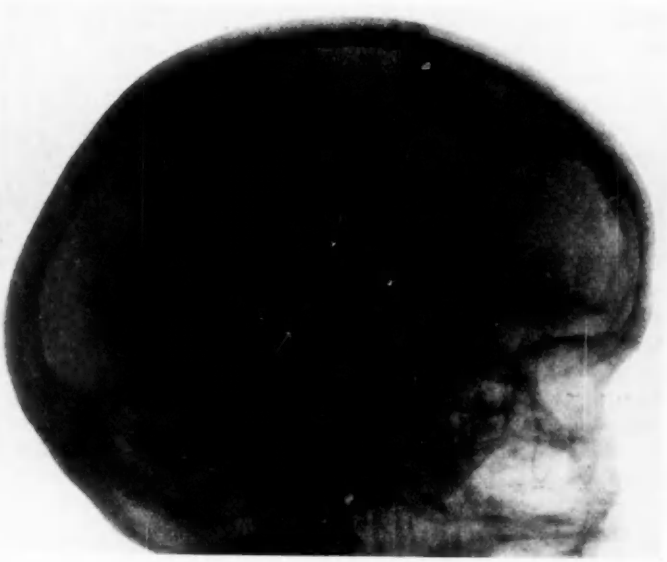

FIG. 4 (*Case* 17).—Radiogram of an intracerebral aneurysm the size of a walnut, on the right middle cerebral artery.

FIG. 5 (*Case* 17).—The aneurysm as removed by operation.

Post-mortem: The tumour was placed in the front part of the temporal lobe, and extended to the point of origin of the Sylvian artery. The tumour, the size of a walnut, consisted of a compact fibrous capsule and was filled with coagulated blood. In several sections of the capsule, it was found to consist of vessel wall with adventitia, a somewhat atrophied and frayed media, together with a thickened, atheromatous and arteriosclerotic intima. There was no sign of syphilis in the vessel wall (see fig. 5).

Microscopic examination of the medulla oblongata, cerebellum and different other parts of the brain show no signs of active inflammation. There were moderate hyaline changes in the vessels, and in the extracerebral vessels (medulla oblongata) moderate arteriosclerosis. The meninges, especially round the medulla oblongata, were thickened. Arteriosclerotic thickening of the aortic valves at their base, and also very marked fibrous thickening of the edge of the mitral valves, were found. The heart was otherwise normal.

There were arteriosclerotic changes stretching from the aortic valves right down to the iliac arteries. In the arch of the aorta a dilatation was seen. The wall was here very thin and at some places covered with cushion-like projections in the intima, at other places cicatricial depressions, partly longitudinal, partly asteroid.

The last case is in several ways rather exceptional, partly from its purely intracerebral position which is rare (I have not been able to find a quite corresponding case in the literature) and partly in regard to the radiograph. Characteristic shadows in radiographs of intracranial aneurysms are described by H. Albl, Algyogi, A. W. Greene, Groedel, Haas, Heuer and Dandy, Odquist, Schintz, Merrill C. Sosmann and Strøm. Sosmann, with a fairly large personal material, obtained shadows in five cases among twenty aneurysms on the internal carotid artery; thus he was able to diagnose them by radiograms in twenty-five per cent. These cases originate from Cushing's tumour material and show how frequently this form of aneurysm causes symptoms of tumour. The remaining instances are merely case reports, and only in the case of Greene was the diagnosis made during life. These cases taken together give a very characteristic picture: a roundish tumour-like formation, which in itself does not give a shadow, but is surrounded by thin, curved, sharply limited outlines, which take a curved or circular course with their concavity central. Sometimes they overlap or lie outside one another, corresponding to different projections of the surface of the aneurysm, as this is seldom perfectly circular, or as a result of the calcium being embedded in layers. Further, there may be other smaller, irregular, indefinite shadows, spread over the formation, their intensity and extension depending on the calcium content of the

aneurysm. According to Albl, an almost closed circle of shadow is characteristic of aneurysm, but the shadows may be curved or made up of several of different curvature. It is their tendency towards a concentric or circular arrangement which is decisive, as a very arteriosclerotic vessel may give an isolated curved shadow (Albl). It is especially the bigger aneurysms which give characteristic radiograms. Sosmann has in one case found a similar picture in an arteriosclerotic dermoid cyst, and possibly an echinococcal cyst might cause a similar picture (*vide* Claessen's radiographs of echinococcus tumours).

In Nos. 9, 13 and 16 of my cases, the brains and aneurysms were radiographed after the autopsy, but in none of these cases were shadows of calcium found. In No. 9 the sella turcica was seen to be normal also. In the case of bleeding from an aneurysm it will unfortunately often be difficult in practice to get an X-ray examination made before death. In the case of local symptoms without signs of hæmorrhage, a positive X-ray picture ought to lead to the right diagnosis.

While the clinical symptoms of intracranial aneurysms vary and often are either not characteristic or are totally absent, they are in not a few cases so characteristic that diagnosis is possible, provided one remembers how relatively frequent aneurysms of the cerebral vessels are. In many cases X-ray examination of the cranium may give valuable support for the diagnosis which is often dependent otherwise on a study of the course and development of the case. Murmurs as specific symptoms of aneurysms will be discussed in detail later.

Ætiology.—In regard to the ætiology of the aneurysm, opinions differ, and are often quite contradictory. In the cases reported here the cause of the aneurysms has been uncertain. Even if an aneurysm first gives symptoms in advanced age, it is difficult to be sure whether it is congenital, or embolic-mycotic (Eppinger), when the underlying disease may no longer be determined, and especially when no microscopic examination of the aneurysm itself is made. Likewise it will be difficult to settle whether an aneurysm is caused by arteriosclerosis, or whether there is merely an arteriosclerotic degeneration of the wall of the existing aneurysm, associated with arteriosclerosis in the other vessels. In some cases, however, the ætiology is obvious.

That aneurysms may occur as a congenital deformity, Busse showed to be probable in 1920 when, out of 400 autopsies, in no less than thirty-nine he could demonstrate by careful examination aneurysmal formations on the anterior communicating artery (i.e., in about 10 per cent.) ; in 43 per cent. of all the cases he found different anomalies here :

simple duplication of the vessels, plexus formations, deficiency in the junction with local hypoplasia of the artery wall and such like. De Vriese had previously made similar observations which later were confirmed by Schmorl and Aschoff (*cited* by Borchardt). On the whole developmental anomalies and variations in the course of the vessels occur frequently in the circle of Willis (Winde, Wyrubow, Parnisetti). Different authors have also found aneurysms in children.

In my Case No. 10, where, in an 11-year-old girl, an aneurysm the size of a pea was found on the basilar artery, and microscopic examination showed the vessel wall to be normal and without cellular infiltration, there can scarcely be any doubt that the aneurysm was congenital. The same histological picture was found in Case 16, that of a woman aged 40 with an aneurysm, the size of a plum, on the internal carotid artery. Here the probability of a congenital origin of the aneurysm was further increased by the existence of an open foramen ovale. In young persons this ætiology is as a rule the most likely, e.g., in Case 1 (a woman, aged 23) and Case 2 (a man, aged 28). But possibly the aneurysm was congenital in other cases too, e.g., Case 15, that of a woman, aged 53, who had had symptoms for thirty-two years and possibly even from childhood.

Lebert showed in 1866 the frequent coincidence between heart-disease and intracranial aneurysms, and Church reported in 1870 the first case of an aneurysm of embolic origin; this through the work of Ponfick (1873) was fixed as a frequent form of intracranial aneurysm. Later work by Eppinger (1887), Wichern (1911), Loewenhardt (1923), Greene (1926), has confirmed this. It is no rare form; of the forty-four cases of Fearnsides, fifteen were caused by infective emboli.

In my material there is no certain case with this ætiology, but perhaps Case 8 belongs here. There is a possibility that embolic aneurysms quickly give symptoms and burst (Esser); therefore they are likely to be observed most frequently in general medical services. If they have existed for a long time, their origin may only be proved by microscopic examination. Possibly some of my apparently arterio-sclerotic aneurysms, or of the cases where it was impossible to determine the ætiology more precisely, had this origin.

Traumata are reported as a cause of intracranial aneurysms, but only a few cases with such a genesis have been published (Hedinger, Menschel, Stilling); these cases are not wholly convincing. Other reported cases are examples of false aneurysms. Further, it is difficult to exclude the possibility that a pre-existing aneurysm became larger,

or produced its first symptoms, after an accident. Traumata are at any rate a very rare cause of intracranial aneurysms (Orth), and I do not suggest it for any of my cases. Esser also assumes that traumatic aneurysms do not occur. No instance is referred to in Stern's article in "Traumatische Entstehung innerer Krankheiten," 2. Aufl., v. J. Schmid.

All aneurysms were originally supposed to be syphilitic (especially by the school of Heller and French authors) but now opinion is very divided. Syphilis was considered to be the ætiological factor in the majority of cases of intracranial aneurysms by Bartholow (1872), Bradford (1903), Lewandowsky (1912); among modern authors by Krabbe and Backer (1922), Comte (1925); but Eppinger (1887), von Hofmann (1894), Fearnsides (1916), Turnbull (1918), Symonds (1923), Borchardt (1925), E. John (1925), Conway (1926), Parker (1926), Zador (1927), Pollach (1928), Esser (1928), Sands (1929) consider it a rare cause, or wholly deny the existence of syphilitic intracranial aneurysms. There is however no doubt that these may occur. In the case of Krabbe and Backer the syphilitic origin was ascertained by histological examination; but, on the other hand, there do not seem to be any cases of intracranial aneurysms in the literature in which spirochætes have been found histologically.

Turnbull especially has proved the rarity of syphilitic aneurysms: there were none in his and Fearnsides' material of forty-four cases. He refers to the fact that syphilis only attacks the small arteries, producing a proliferative obliterating endarteritis, which hardly ever causes weakening of the vessel wall and dilatation, except secondarily in the larger arteries through affection of the vasa vasorum. Saadhoff considers that syphilitic aneurysms are mostly found on the basilar artery.

The importance of arteriosclerosis in the causation of intracranial aneurysms is also disputed. It was assumed as a causative factor by Eppinger (1887) ?, Burns, Fearnsides (1916), Turnbull (1918), and Kerpola (1919); while others (e.g., Hofmann and Comte) contradict this view. On the other hand A. Jakob has recently maintained that arteriosclerosis gives rise to the formation of aneurysms and afforded histological demonstration of this. In reality arteriosclerosis is surely a frequent cause of aneurysms, as especially shown by Kerpola.

The attempt to distinguish between syphilitic and arteriosclerotic disease of the cerebrospinal blood-vessels by the pathologico-anatomical picture alone has led different observers to hold contradictory

views. Without further discussion of this disputed question I shall merely state that A. Jakob in his new book maintains that amongst the changes of the vessels of the brain which are classed as arteriosclerotic in the usual sense, lesions of syphilitic origin occur and he places syphilitic arteriosclerosis as a special form of this (A. Jakob: "Anatomie und Histologie des Grosshirns," Bd. 1, Leipzig, 1927, p. 353).

Among my cases there are four in which syphilis had been proved, or the lesions revealed at autopsy suggested syphilis. Three had lues of the nervous system, while the fourth during the course of her lues in early life had a hemiplegia which had passed off without leaving symptoms.

The most evident case is No. 13 in which there was encephalopathia luica (endarteritis obliterans), syphilitic aortitis with ectasia aortæ and arteriosclerotic changes in the coronary arteries, associated with a spindle-shaped aneurysm on the basilar artery (see fig. 1). The microscopic examination of the aneurysm showed a hyaline arteriosclerotic thickening of the intima which continued into the distended part of the vessel. The elastic tissue in the media could only be faintly seen. Inflammatory processes were absent both in the media and the adventitia, and there were no changes in the small vessels of the adventitia. But on section of the internal carotid artery, intimal thickenings due to perivascular infiltrations of round cells were found, and there was some thickening of the small vessels in the adventitia.

Without entering into the relationship between syphilis and arteriosclerosis (especially in the central nervous system) it is quite justifiable to maintain that the histological appearances in the aneurysm by no means prove its syphilitic origin, but are rather in favour of arteriosclerosis. A similar picture of typical arteriosclerotic changes was seen in the aneurysm in Case 17. In the wall of the vessel no signs of syphilis were found, but the autopsy showed a combination of arteriosclerotic and syphilitic changes in the aorta, which was the seat of an ectasia. The hemiplegia which occurred in the forty-fifth year had probably been on a luetic basis; at any rate the lesion was in the opposite hemisphere to the aneurysm.

In the third case, that of a woman, aged 59, with lues spinalis (tabes?), a ruptured aneurysm the size of a pea was found on the internal carotid artery, together with universal arteriosclerosis, but no definite signs of syphilis, certainly none in the aorta. The character of the aneurysm cannot be determined now.

In a fourth case, in a 64-year-old woman (Case 11), who had died

from an encephalomalacia, an unburst, thin-walled aneurysm, almost the size of a plum, on the ophthalmic artery was discovered accidentally by autopsy. Universal arteriosclerosis was found, especially in the aorta, but no sign of syphilis. Clinically she presented the picture of two cerebral softenings occurring at an interval of a couple of months. Wassermann reaction in the blood positive (0.0.0.0.100), in the spinal fluid positive (0.0.20.100). The nature of the aneurysm cannot be determined.

In a fifth previously reported case (No. 14), in a 66-year-old man, there was a considerable ectasia of the very arteriosclerotic basilar artery, together with considerable arteriosclerosis of the aorta, which at one place in the thoracic portion resembled a syphilitic aortitis. On microscopic examination of this part pronounced thickening of the intima was found and arteriosclerosis along the edge of the media in which there were doubtful inflammatory changes. Clinically there was no information about syphilis, and unfortunately neither lumbar puncture nor a Wassermann reaction was performed.

In these four cases of intracranial aneurysms in patients with cerebrospinal lues, there was in none definite proof that the aneurysm was syphilitic. Whether the syphilis might have had any influence on the development of the arteriosclerosis, as maintained by Bradford, cannot be discussed here.

In my material there is a series of aneurysms with arteriosclerotic changes, but whether the aneurysm or the arteriolsclerosis is the primary is not easy to determine. An already existing aneurysm may, like other vessels, undergo atheromatous degeneration, but there seems to be no reason why the aneurysm should be especially exposed to this (e.g., on account of abnormal circulation), the causation of arteriosclerosis is usually assumed to be an autotoxic action on the vessel wall (cholesterinæmia). Thoma, however, ascribes a certain importance to the conditions of the circulation (see later). On the other hand arteriosclerosis is so capricious in its localization and extension that a local, limited arteriosclerosis must be considered as the cause of the formation of an aneurysm, as in the following case.

Case 18.—Woman, aged 64. Died December 8, 1917.

The clinical history was of no interest (simple rupture of the aneurysm with paralysis of the oculomotor nerve).

Autopsy revealed no marked sclerosis of the vessels on the base of the brain. On the lower side of the left temporal lobe a ragged tumour the size of a walnut, of very compact consistency, was found. On incision it was seen to

consist of old coagula in layers, surrounded by a thin shell, which continued in a central direction into the left Sylvian fissure. The Sylvian artery, 4 cm. from its origin from the internal carotid artery, suddenly developed arteriosclerotic changes, and became enlarged to an aneurysm the size of a walnut. In the rest of the brain there was a smoothing of the gyri especially in the left hemisphere, but no focal changes. It is strange, in this case, to find isolated arteriosclerotic changes localized symmetrically and exclusively to the two Sylvian arteries, and going on to the formation of an aneurysm only on the left side.

In others of my cases the wall of the aneurysm has shown obviously arteriosclerotic changes, while the rest of the cerebral vessels did not reveal any sign of arteriosclerosis on microscopic examination. Thus in Case 9 there were arteriosclerotic changes, thickenings of the intima, calcification and disintegration of the media, but no trace of inflammatory lesions. There were also slight arteriosclerotic changes in the aorta, but not in the rest of the vessels.

Busse also considers that arteriosclerosis plays a certain part in the formation of aneurysms on the anterior communicating artery and admits that some aneurysms only appear after the age of 40. Turnbull, on the other hand, assumes a congenital weakening of the media as the cause of arteriosclerotic aneurysms, which he considers are common, and more frequent on the intracranial arteries than elsewhere. Even if congenital abnormalities or weakness form loci minoris resistentiæ, the importance of atheroma is indisputable.

Thoma held that primary increase of the lumen of the vessel played a definite part in causing arteriosclerosis, and considered the proliferation and thickening of the intima as an arrangement for preserving the size of the lumen (an illustration of this has been reproduced by Osler). But these views do not seem to have gained general acceptance.

In cases of diffuse universal arteriosclerotic changes in the vessels of the brain, the arteriosclerosis is probably the sole cause of the aneurysm. Thus in Case 22, besides a ruptured aneurysm the size of a pea on the right Sylvian artery, there was considerable arteriosclerosis of limited portions of the vessels. In many of the cases the cerebral arteriosclerosis was diffuse, but so pronounced that it was a plausible explanation of the aneurysm.

A rather characteristic histological picture was present in Case 12 where, in a 75-year-old man with a senile, arteriosclerotic dementia and considerable universal arteriosclerosis, an unburst aneurysm was found on the basilar artery, about 2 by 1½ cm. in size. Microscopic examination

of the aneurysm showed that its wall consisted in large part only of adventitia in other places also of intima together with broken plaques of media. The whole lumen was completely filled up with thrombotic masses. In the best preserved part of the vessel wall arteriosclerosis was seen in the intima and slight infiltration of round cells in the adventitia. The latter is probably associated with the absorption of the thrombotic masses (Paul Møller).

FIG. 6 (*Case* 12).—An arteriosclerotic aneurysm of the basilar artery which was found at autopsy in a man who died with senile dementia and softening of the cerebellum. The aneurysm measured 2 × 1½ cm. and was filled with a stratified clot.

Thus of my twenty-three cases four are found in persons with syphilis in the central nervous system (*vide supra*). Of the remaining nineteen, eleven are classed as arteriosclerotic, since they showed undoubted arteriosclerotic changes either microscopically or macroscopically, and no evidence of any other origin was found. Even if in one or two of these there may have been some other cause, the number is still remarkably large. Fearnsides also found a remarkable number of arteriosclerotic aneurysms. In addition five (as already mentioned) are congenital, and one perhaps infectious (embolic-mycotic, Eppinger), while the cause of the two last cases is uncertain. The probability is that arteriosclerotic aneurysms are frequent and aneurysms of undoubtedly

syphilitic origin are relatively rare. Corresponding with this, C. H. Sattler, among 352 cases of exophthalmos, only found one case of syphilitic origin. Thus the finding of tertiary syphilis has no diagnostic value, as maintained by Krabbe and Backer.

Noises in the head, which these authors mention as a diagnostic point, are unfortunately rare. They are but rarely observed, and are not in any way pathognomonic, as they are also found in tumours compressing larger vessels (Zador), in anæmic women (Oppenheim), in Graves' disease (Gowers) and in arteriosclerosis of the vessels of the brain (Wallenberg), although in this case they may be due to a small aneurysm. This phenomenon is a subjective feeling of ringing or pulsation, "like a machine working inside the head;" the sound is said to be also distinctly heard on auscultation of the cranium with a stethoscope. In cases of arterio-venous aneurysm between the internal carotid artery and the sinus cavernosus noises in the head are common (Ehlers). Bing reported a case of presumed intracranial aneurysm (not verified by autopsy); a 17-year-old woman who suffered from disease of the heart, presumably caused by a patent ductus Botalli, heard a pulsating jangle especially in the right ear; the sound could not only be auscultated over the whole cranium, but was also to be heard at a distance of 8 cm. Another characteristic symptom was mistiness of vision increasing to short attacks of blindness on effort, for example, when she sat up in bed.

Dr. E. Warburg has demonstrated to me a rather similar case, and has been so kind as to put it at my disposal, for which I wish here to offer him my best thanks. In this case I feel quite justified in making the diagnosis of intracranial aneurysm.

Case 24.—69-year-old landed proprietor.

The patient is a vigorous man, who looks much younger than his age; the greater part of his life he has lived in the country under good conditions; he is a moderate smoker and has never taken wine to excess. Has never had syphilis. Wassermann reaction negative. From his youth onwards he has had very severe "rheumatic" myalgia for which he has been treated several times with physiotherapy. In 1923 he had a long febrile attack with violent myalgia, for which he was treated at a health resort for three months with sulphur oil injections. His condition became considerably better, his temperature returned to normal, and after a stay in Gastein he felt almost cured.

In August, 1928, the patient had a typical attack of gout in both hands, which vanished in a few weeks under treatment with atophan. He then felt completely well till early in 1929 when he and his wife got a slight febrile

infection called influenza; a couple of weeks later he began to get extremely violent pains which radiated from his left ear up into the scalp. Some weeks later similar pains occurred in the right side of the head. The patient was extremely sensitive to changes of temperature and had great tenderness of the scalp, though perhaps not in the neck. Both temporal arteries were firm and thickened; later during the disease first the left temporal artery and then the right thrombosed, and became pulseless; now nine months after the onset of the disease, the pulse is still absent from the right one and only doubtful in the left. The patient was slightly febrile with temperatures between 38° and 38·5° C. for two to three months; he was in great pain and had much aspirin, atophan, allonal, cibalgin, quinine, &c., but it was not necessary to use morphia. Among the numerous antineuralgic remedies used only aspirin seems to have had any definite effect; he had up to 8 grm. in twenty-four hours. In addition he was treated with courses of sudorifics. The patient became much weaker during this period; he suffered very much from perspiration, ate only very little, and lost 6 kg. in weight. After two to three months the pains grew less and he got out of bed.

As the diagnosis was difficult, the patient was examined by Dr. K. H. Krabbe for neurological signs, by Dr. Frants Norsk for evidence of disease of the ear or throat, and by Dr. Collin who radiographed his cranium, but nothing further was discovered.

During the disease an anæmia developed which was treated by injections of arsenic without effect; only when in June and July he went into the country, and at the same time began to eat powdered liver, did a remission take place.

Date	Hb.	Erythrocytes, million	Erythrocytes, vol.	Index, colour	Index, vol.
24/4	76 per cent.	3·9	29·5	0·97	0·87
1/5	66 ,,	3·9	34	0·83	1·01
3/6	65 ,,				
30/8	83 ,,				

During the summer the pains disappeared completely, and he was completely all right, and even partook in many parties, considering his age.

One day in August he suddenly had a feeling as if he had a one-cylinder motor in his head and at the same time, or almost at the same time, a cloud over the right eye. There was no pain and the condition of the patient was otherwise unchanged.

Ophthalmic examination by Dr. Fabricius-Jensen showed his visual acuity to be $\frac{5}{6}$. The right pupil was a little bigger than the left, but reacted normally. Ophthalmoscopy showed fine senile degeneration in the retina, but nothing pathological. Tension normal. In the right field of vision there was a complete paracentral scotoma for white and colours, and in continuity with this a relative scotoma with indefinite edges. The outer boundary for white and red was normal. The blind spots were of normal size (see fig. 7). The left field of vision was normal.

At the end of September Dr. Warburg again examined the patient, and he was now able, when he placed his ear to the patient's ear on either side, to hear plainly a soft noise, synchronous with the pulse. The noise could only be heard directly on the ear, and is of equal force on both sides; it could not be heard with the tube-stethoscope.

The blood-pressure is 120/60; examination of heart, even by an electro-cardiogram, shows nothing abnormal; no special sclerosis of the brachial arteries exists.

There has been no dizziness during the disease, except a few times when he was very anæmic; no vomiting, no tachycardia or bradycardia and no paresis.

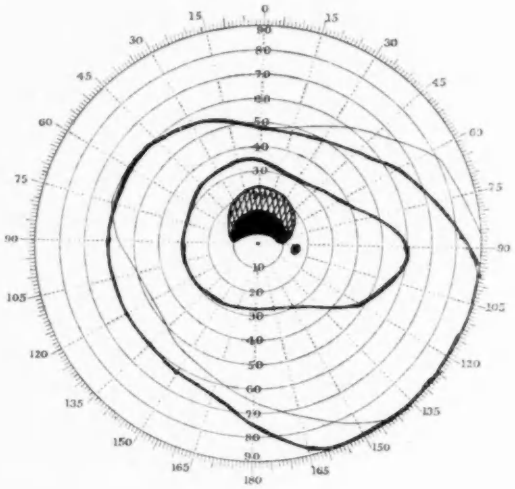

FIG. 7.

The condition has since remained unchanged and the scotoma is stationary; the noise is still heard distinctly directly by the ear, equally strongly on both sides. There are no symptoms on effort or congestion of the head.

In this case the diagnosis of an intracranial aneurysm (assumed to be on right internal carotid artery) is fairly certain, in view of the thrombosis of different vessels of the head and severe pains developing in connection with a prolonged febrile disease; later, subjective and objective intracranial murmurs appeared and a scotoma in one eye. It may be supposed that the aneurysm at this moment suddenly had developed to its full size. It is probable that after the resorption of the thrombotic mass the wall of the vessel, weakened locally by inflammation, has been no longer able to resist the arterial pressure and dilated

into an aneurysm, which compresses the optic nerve. Apart from the murmur the patient is now subjectively well.

It is noteworthy that the blowing noise could only be heard on direct auscultation, and not with a stethoscope: this has not previously been reported in the literature. This may perhaps explain why murmurs are so seldom noted in cases of aneurysms on the cerebral vessels, but it is probable that so unpleasant a symptom would have been complained of by the patient and, if really a frequent symptom, would not have escaped mention. In future it will be advisable to auscultate the cranium directly, in any case where the possibility of a brain aneurysm exists. Bing tries to explain the audible murmur by the fact that the aneurysms are nearly always placed on the base, and therefore the sound is conducted directly by bone especially through the great wing of sphenoid; but evidently this is not the explanation, at any rate not in the present case.

Treatment.—The therapy of intracranial aneurysms has until now only given very poor results, which is mainly due to the difficulties of diagnosis. In some cases operative intervention has been tried, usually on the supposition that a tumour was present. In one case Cushing vainly tried to remove an aneurysm; later he ligatured the internal carotid artery instead, but this treatment caused hemiplegia, which partly disappeared later. Ranjard is said in two cases to have gained good results by ligature of the intracranial part of the internal carotid artery, and Coe and Lefort have also successfully used operative treatment. Forster (after Borchardt) has in one case been successful by a decompressive craniotomy. In view of the serious prognosis of aneurysms, at least when signs of hæmorrhage or impending rupture are present, operation is justified; when hæmorrhage has occurred the result will possibly be doubtful. The best method is ligation of the supplying vessel, especially the internal carotid artery after temporary compression of the common carotid artery in the neck, to avoid a hemiplegia. In cases of pulsating exophthalmos where, however, circumstances are not quite the same, this treatment has not always given satisfactory results. Extirpation of an intracranial aneurysm with good results has not been reported in the available literature, even though in several cases it might have been technically possible (Borchardt).

On account of the diagnostic difficulties therapy must, as a rule, be conservative, which most frequently means preventive. Gelatine injections may possibly have some effect in bleeding aneurysms. Lumbar puncture, although of therapeutic importance in other forms of sub-

arachnoid hæmorrhage, surely ought to be carried out with the utmost caution and reserve. Sudden death has followed it, and in my Case 9 the operation seems to have an unfavourable influence on the hæmorrhage.

It is to be hoped that in future a greater knowledge of the clinical features of intracranial aneurysms and their characteristic X-ray appearances will enable the diagnosis to be made more frequently, and that the way will thus be opened for therapeutic procedures.

I am much indebted to my chief, Professor Wimmer, for his permission to publish the material from the Department, to prosector Dr. L. Melchior for his permission to use the pathologico-anatomical material, and to the chief of the X-ray clinic, Dr. G. Biering, for his permission to publish the X-ray photos.

Addendum.

After this work was completed a new case of ruptured intracranial aneurysm (diagnosed *intra vitam*) occurred in the Department for Mental and Nervous Diseases at the Kommunehospital.

This case is of great interest as a supplement to the preceding, the aneurysm being so small that only a very carefully performed autopsy revealed it.

A married man, aged 38, was admitted to the Department for Mental and Nervous Diseases in the Kommunehospital on February 11, 1930, and died there two hours later.

He had syphilis twelve years ago and was at that time treated in the Department for Skin and Venereal Diseases at the Kommunehospital. For many years there was incessant abuse of alcohol, which suddenly ceased two months ago when he was out of work. Otherwise he had been healthy.

During the last month he had complained of a headache. About two hours before admission he came home complaining of a severe headache. He went to bed, but a moment later got up again complaining of a rather strange taste in his mouth, and shortly after he fell unconscious to the floor. Soon after this he had convulsions.

When admitted he was still in convulsions, but they soon ceased. He was unconscious, pale and slightly cyanotic. The rectal temperature was 37·1° C., respiration bout 20, rattling, slightly snoring; pulse 76, regular, strong; blood-pressure 150/90. The pupils on both sides were rather dilated and did not react to light. The right eye was slightly divergent outwards and upwards. Ophthalmoscopic examination showed the edges of the optic discs normal, perhaps a little blurred; the vessels curved, twisted and distended.

Lateral and medial to the right optic disc smaller and larger hæmorrhages were seen close to it.

There was pronounced rigidity of all four extremities. He was inclined to keep the arms rotated inwards; the deep reflexes were equal and lively with a tendency to clonus; a Babinski response was obtained on both sides; there was no stiffness of the neck; the abdominal reflexes were feeble or absent. Other examinations showed nothing special.

He died rather suddenly two hours later.

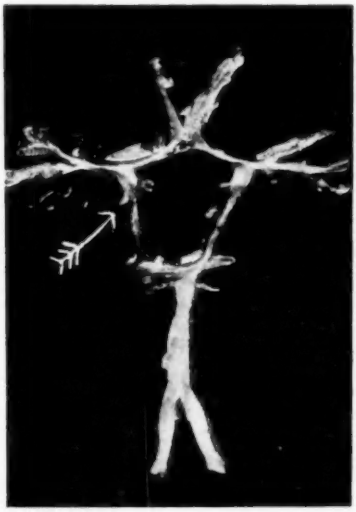

FIG. 8 (*Case* 25).—A ruptured aneurysm the size of a millet seed on the right internal carotid artery.

The autopsy fifty-six hours later at the Institute of Medical Jurisprudence showed his tongue had been bitten. A considerable subdural hæmorrhage was found, especially on the right side, with large coagula below and outward. There was also a considerable hæmorrhage in the soft membranes, most pronounced round the pons and chiasma, on the lower side of the cerebellum and at the beginning of the medulla oblongata. It was fairly symmetrical; there was less laterally and none on the convex surface of the brain. At the apex of the right temporal lobe and on its basal surface an irregular opening was found, admitting a little finger: from this one came into a superficially placed cavity, about the size of a hazel-nut and filled with blood. The walls of this cavity consisted of fairly fresh brain-tissue with diffuse punctate or streaky infiltration by blood.

After the coagula had been carefully removed, an aneurysm the size of a

millet-seed and with thin walls was revealed on the right internal carotid artery and on the middle cerebral artery. At the root of this aneurysm a very fine irregular rupture was found which admitted only a very fine probe (fig. 8). Atheromatous spots were found on the basilar artery and on the internal carotid artery. There were arteriosclerotic changes in the aorta.

This case is instructive as it shows the necessity of making a minute and careful examination of the extracerebral vessels for ruptured aneurysms in cases of subarachnoid hæmorrhage.

I am much indebted to Professor Dr. K. Sand for his permission to use the description of the autopsy and to take photographs of the preparation.

LITERATURE.

ALBL, H. *Fortschr. Röntgenstr.*, **39**, 890 (1929).
ALGYOGI. *Ibid.*, **14**, 257.
BABINSKI, J., and JUMENTIÉ, J. *Bull. et Mém. de la Soc. méd. des Hôp. de Paris*, 744 (1912)
BARTHOLOW, ROBERTS. *Amer. Journ. Med. Sci.*, **64**, 373 (1872).
BEADLES. *Brain*, **30**, 285 (1907).
BING, H. J. *Bibl. f. Laeger.*, **114**, 217 (1922).
BORCHARDT, MORITZ. *Bruns' Beitr.*, **133**, 429 (1925).
BRADFORD, JOHN ROSE. *Lancet*, **86**, ii, 703 (1908).
BRUNS. "Die Geschwülste des Nervensystems," 2. Aufl., 59 (1908).
BUSSE, OTTO. *Virchow's Arch.*, **299**, 178 (1921).
CHURCH, W. S. *St. Bartholomew's Hosp. Records*, **6**, 99 (1870).
CLAESSEN, GUNNLAUGUR. *Acta Radiolog.*, Suppl. IV (Stockholm, 1928).
CÖE. *Gaz. méd. des Hôpitaux*, 495 (1856). Cited by BORCHARDT.
COMTE, A. "Nouveau Traité de Médecine" (Roger-Widal-Teissier), **19**, 415 (1925).
CONWAY, J. A. *Brit. Journ. of Ophthalmol.*, **10**, 78 (1926).
CUSHING, HARVEY. *Guy's Hosp. Records*, **73**, 159 (1923).
DEMAY, IVAN BERTRAND, and PERISON, J. *Rev. Neurol.*, **33**, i, 1027 (1926).
DUPUY-DUTEMPS. *Annales d'Oculistique* (March, 1914).
EHLERS, HOLGER. *Acta Psychiatr. et Neurol.*, **4**, 151 (1929).
EPPINGER, HANS. *Arch. f. klin. Chir.*, **35**, Suppl. (1887).
ESSER, A. *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, **114**, 208 (1928).
FEARNSIDES, E. G. *Brain*, **39**, 224 (1916).
FLATAU, E. *Gaz. des Hôpitaux*, 1077 (1921).
GOLDFLAM, S. *Deutsch. Zeitschr. f. Nervenheilk.*, **76**, 158 (1923).
GOUGUENHEIM. *Thèse de Paris*, 1866.
GOWERS, W. R. *Deutsch. ausg. v. Karl Grube*, Bd. II, 525 (Bonn, 1892).
GREENE, A. W. *Journ. of Ophthal., Otol. and Laryngol.*, **30**, 106 (1926). Ref. *Zentralbl. f Neurol. u. Psychiatr.*, **46**, 193 (1927).
GREEN, F. H. K. *Quart. Journ. of Med.*, **21**, 419 (1928). Ref. *Zentralbl. f. d. ges. Neurol. u. Psychiatr.*, **50**, 579 (1928).
GROEDEL. "Röntgendiagnostik in der inneren Medizin," *Lehmann's mediz. Atlas*, Bd. **7**, II, 285 (1914).
GUILLAIN, GEORGES. "Traité de Pathologie médicale et de Thérapeutique appliquée." V. Neurologie, **1**, 569 (1925). (Sergent-Ribadeau-Dumas-Babonneix.)
GUILLAIN, G., and VINCENT, CL. *Semaine méd.*, 505 (1909).
GULL, WILLIAM. *Guy's Hospital Records*, **5**, 281 (1859).

HAAS. *Fortschr. Röntgenstr.*, **33**, 469 (1926).
HARRIS, S. TAYLOR. *Brit. Journ. of Ophthalmol.*, **12**, 15 (1928).
HASSIN, G. B. *Arch. of Neurol. and Psychiatr.*, **17**, 770 (1927).
HEDINGER. *Korresp.-Bl. f. Schweiz Aerzte* (1917). Cited by BORCHARDT.
HEUER, G., and DANDY, W. *Johns Hopkins Hosp. Records*, **27** (1916).
VON HOFMANN, E. *Wien. klin. Wochenschr.*, **7**, 823, 848, 867, 886 (1894).
INGVAR. *Nouv. Icongr. de la Salpêtr.*, **28**, 313 (1919).
JOHN, EMIL. *Deutsch. Zeitschr. f. Nervenheilk.*, **86**, 250 (1925).
KARPLUS. *Arb. a. d. Wiener neurol. Inst.*, **8** (1902).
KERPOLLA, W. *Arb. a. d. patholog. Inst. Helsingfors N.F.*, **2**, 15 (1919).
KRABBE, KNUD H., and BACKER, KAJ H. *Acta medica scandinavica*, **56**, 95 (1922).
KREY. "Ein Fall von Aneurysme der Art. cerebelli sup. ant.," Inaug. Dissert., Greifswald, 1891.
KÜMMEL. *Münch. med. Wochenschr.*, **58**, 1293 (1911).
LANGE, CARL. *Hospitalstidende*, **15**, 205 (1872).
LEBERT, H. *Berl. klin. Wochenschr.*, **3**, 208, 229, 249, 281, 336, 345, 386, 402 (1866).
LEWANDOWSKY, M. "Handbuch der Neurologie," Bd. **3** (Spez. Neurol. II), 101 (1912).
LOEWENHARDT. *Deutsch. med. Wochenschr.*, 439 (1923).
MENSCHALL. *Aerztl. Sachverst.-Zeit.*, **28**. Cited by BORCHARDT.
MOORE, R. FOSTER. *Trans. Ophth. Soc. United Kingdom*, **45**, 490 (1925).
MUNCK, WILLY. *Hospitalstidende*, **69**, No. 7 (1926); *Journ. Nerv. and Ment. Dis.*, **65**, 483 (1927).
MØLLER, HARALD. *Bibl. f. Laeger.*, **112**, 73 (1920); *Zentralbl. f. d. ges. Chir.*, 138 (1920).
MØLLER, PAUL. *Hospitalstidende*, **64**, 305 (1921); *Zentralbl. f. d. ges. Chir.*, 518 (1921).
ODQUIST, H. *Acta Med. Scand.*, **63**, 286 (1926).
OSLER, W. "Aneurysm," Osler's "Modern Medicine," **iv**, 459 (1908).
OPPENHEIM, H. "Lehrbuch der Nervenkrankheiten," 6. Aufl., **ii**, 1226 (Berlin, 1913).
PARKER, H. L. *Arch. Neurol. and Psychiatr.*, **16**, 728 (1926).
PEDERSEN, THORVALD. *Hospitalstidende*, **64**, 721 (1921).
PETRÉN, KARL. *Deutsch. Zeitschr. f. Nervenheilk.*, **10**, 308 (1928).
PINCHERLE, PINO. *Fortschr. Röntgenstr.*, **29**, 315 (1922).
NEWTON PITT, G. *Brit. Med. Journ.*, **1**, 827 (1890).
PEACOCK. *St. Thomas's Hosp. Reports*, New Series, **7**, 119, 317 (1876).
POLLOCK, LEWIS J. *Med. Clin. of North America*, **11**, 1 (1927). Ref. *Zentralbl. f. Neurol. u. Psychiatr.*, **46**, 660 (1928).
PONFICK. *Virchow's Archiv.* **58**, 528 (1873).
RANJARD. *Arch. internat. de Laryngol., Otol., Rhinol. et Broncho-œsophagoscop.*, **1**, 330, cit. by BORCHARDT.
REDLICH, E. Lewandowsky: "Handbuch der Neurologie," Bd. **3** (Spez. Neurol II, 549, 565, 617, 627 (1912).)
REINHARDT. *Mitteil. a. d. Grenzgeb. d. Med. u. Chir.*, **26**, 432 (1913).
RIDDOCH, G., and GOULDEN, C. *Brit. Journ. of Ophthalmol.*, **9**, 209 (1925).
SAADHOFF. "Beitrag zur Pathologie der Art basilaris," *Deutsch. Arch. f. klin. Med.*, **84**. 384 (1905).
SANDS, IRVING J. *Arch. of Neurol. and Psychiatr.*, **21**, 37 (1929).
SATTLER, C. H. "Graefe Saemish Handbuch der gesamte Augenheilkunde."
SCHINZ. Cited by ALBL.
SCHRØDER, G. E. *Bibl. f. Laeger*, **111**, 319 (1919).
SCHÜLLER. Cited by STRØM.
SHORE, BENJAMIN RICE. *Arch. of Neurol. and Psychiatr.*, **21**, 609 (1929).
SIMMONDS. *Deutsch. med. Wochenschr.*, **27**, 353 (1901).
SLOMANN, H. C. "Bidrag til Læren om den pulserende Exophtalmus," Disputats, Kbhvn., 1898.
SOSMAN, MERRIL C. *Brit. Journ. of Radiol.*, **30**, 468 (1925).
SOUQUES, A. *Nouv. Icongr. de la Salpêtr.*, **21**, 108 (1908).

STRØM. *Fortschr. Röntgenstr.*, **27**, 577 (1921).
SYMONDS, C. P. *Guy's Hosp. Reports*, **77**, ser. iv, vol. iii, 139 (1923).
Idem. Quart. Journ. of Med., **18**, 93 (1924).
THOMA, R. *Virchow's Archiv*, **104**, 408; **111**, 76; **112**, 259; **113**, 244, 505.
Idem. Ibid., **245**, 78 (1923).
THOMAS, HENRY M. Osler's "Modern Medicine," **7**, 339 (1910).
TURNBULL, HUBERT M. *Brain*, **41**, 50 (1918).
DE VRISE, BERTHA. *Arch. de Biol.*, **21** (1905).
WICHERN, HEINRICH. *Münch. med. Wochenschr.* (1911); *Deutsch. Zeitschr. f. Nervenheilk.*, **44**, 220 (1912).
WINDLE, BERTR. C. A. *Journ. Anat. and Physiol.*, **22**, 289 (1888).
ZÁDOR, JULIUS. *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, **109**, 716 (1927).

Notices of Recent Publications.

Die diagnostische Bedeutung des Rossolimoschen Reflexes bei Erkrankungen des Zentralnervensystems. von S. Goldflam. S. 274. Berlin: S. Karger. 1930. Price 24 M.

A consequence of the selective incidence of hypertonus in the extensors and plantar flexors of the lower limb in lesions of the pyramidal system is that percussion of any part of the foot elicits a "stretch reflex" of the plantar flexors of the toes, with a down-going movement of the toes. The phenomenon has the same significance as a heightening of the tendon-jerks obtained elsewhere in the limb.

It is clear that one can chose any one of a great number of spots on the foot from which to elicit this response, but that in each case the reaction is the same one, and that there is no justification in naming a series of different "reflexes" simply because a single response is elicited from different parts of the receptive field.

Unfortunately, this is what has occurred and a very simple matter has been rendered unnecessarily complicated and mysterious as a consequence. Rossolimo found that the response could be elicited by percussion on the sole of the foot over the balls of the different toes, and thus neurological literature had been endowed with Rossolimo's reflex. Bechterew, percussing the point of the heel, discovered Bechterew's heel reflex. Two observers, choosing the site of extensor brevis digitorum on the dorsum of the foot gave us the Mendel-Bechterew reflex, while Shukowski preferred the middle of the sole and Shukowski's reflex is the result.

It is to be hoped that with the greater knowledge of the physiology of the tendon reflex that is now available, this undesirable and unscientific practice of attaching the names of individuals to these reflex phenomena, and of regarding the latter simply as mysterious diagnostic symbols, will cease, and that a more rational outlook will be adopted.

Goldflam is not, however, concerned with the physiology of the Rossolimo phenomenon, but simply with its value as a diagnostic trick for the early recognition of pyramidal affections. He records in the present monograph its occurrence throughout the wide range of known affections of the nervous system, and compares its value from this point of view with that of the Babinski phenomenon. He concludes that it is sometimes present before the latter makes its appearance.

The book is very diffusely written, frequently deviates into topics quite unrelated to its title, and includes numerous case records that are too incomplete to be of any value.

Syphilis héréditaire du Système nerveux. Par L. Babonneix. Pp. 429. Paris: Masson et Cie. 1930. Price 60 francs.

The author has collected and arranged within the present volume his numerous published contributions upon the subject of hereditary neurosyphilis. Designedly, he has produced not a formal treatise upon the subject, but a documented exposition of his view that hereditary syphilis plays a fundamentally important part in the causation of a great number of the neurological disorders of infancy and childhood.

His inclusion of Sydenham's chorea within these disorders will indicate how widely he has cast his net, and also upon what scanty evidence he is at times prepared to find confirmation of his views. In fact, throughout the book, which contains very numerous case summaries, the reader will be struck by the tenuous character of the evidence upon which the author is ready to invoke hereditary syphilis.

It is, perhaps, as an exhaustively elaborated piece of special pleading, in favour of the conclusion that hereditary syphilis plays an almost universal rôle in the causation of chronic neuro-muscular disorders in early life, that the book will have its chief interest for the experienced neurologist.

Techniques histologiques de Neuropathologie. Par Ivan Bertrand. Pp. 376. Paris: Masson et Cie. 1930. Price 50 francs.

This volume on neurohistological technique does not purport to be a complete record of all the methods which have been used for the study of the nervous system But it is none the less remarkably complete and up to date. The methods are clearly and fully set out, and reference back to other methods is as far as possible avoided. The last sections, dealing with the staining of degeneration products, glycogen, calcium, iron and blood derivatives, are particularly useful. The section on Marchi's method also gives some valuable advice on the recognition of artefacts, but less help than might have been hoped for in avoiding them. One is tempted to criticize the method recommended for cutting off the skull-cap by means of chisel and hammer only, without using the saw. It is also remarkable that a solution of formalin in water rather than in saline is still used in the laboratory of the Salpêtrière.

It is disappointing to note the omission of many of the useful tips which were to be found in the little book on the same subject by Roussy and Lhermitte. Such were the use of acid balsam for preserving the colour of Van Gieson's counterstain and of cedar-wood oil as a mountant for Nissl sections. The author's technique for the use of infra-red light to bring out certain of the finer points in the structure of nerve-cells appear to be too complicated for any but special research work, but it is valuable to have it incorporated in this book. Taken as a whole the book includes so much that is new or scattered in foreign journals that it is a valuable addition to the library of any research worker in neuropathology.

Études neurologiques. Troisième Série. Par G. GUILLAIN. Pp. 543. Paris: Masson et Cie. 1929. Price 70 francs.

The two preceding volumes in this series have already been noticed in this Journal, and like them the present volume contains a number of clinico-pathological studies, cast in the form of lectures and articles, and taken at random from the whole field of neurology. By design new and original work is excluded from the series. The majority of the thirty-three studies have already been published in medical journals.

They are of interest in that they exemplify the manner of approach adopted at the Salpêtrière in the investigation, and demonstration to students, of clinical material.

Die Röntgenbehandlung der Nervenkrankheiten. Von O. MARBURG und M. SGALITZER. S. 213. Berlin: Urban und Schwarzenberg. 1930. Price 15 M.

The authors provide an exhaustive review of the literature of the treatment of the various affections of the nervous system by Röntgen rays. The volume is divided into a general and a special section. In the former, full technical details of the treatment of nervous diseases is given, while in the latter under clinical headings are grouped a review of the literature, case records and complete information as to dosage and modes of application. An admirable and critical summary concludes each such section. There is a comprehensive bibliography.

The book may be recommended as of value to the neurologist and to the radiotherapist.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. Sechster Band, Spezieller Teil II. Berlin: Springer. 1928. S. 376. Price Rm. 37.70.

This volume of Bumke's Handbuch contains two authoritative monographs. In the first Professor Lange presents the sum of our present knowledge concerning the affective psychoses and related conditions. As the pupil and colleague of Kraepelin, he naturally accepts the general Kraepelinian nosology, but with appropriate and adequate adaptation to modern notions. On many points he has put forward less rigid and dogmatic views than in his own earlier writings; this is evident, for example, if one contrasts his 1926 paper on melancholia with many passages in the present work. There can be no doubt that this will take the place of Stransky's earlier monograph; it is complete, and thorough to a fault.

The second part of the volume, devoted to paranoia and related conditions, is by Professor Kehrer. It is written from a definite personal standpoint, but anyone who has wandered through the wilderness of paranoia literature will

welcome this. It is predominantly clinical, with illustrative case histories; the relevant literature is appraised in its degree. It is impossible to consider here his delimitation of the paranoia concept to cover only disorders in which the mental picture is more or less restricted at all times to logically grounded delusions entirely comprehensible as to motive and content; it is at any rate acceptable and precise, like the rest of the monograph. There is no glossing over difficulties or offering of fanciful solutions.

Die Prognostik der Endogenen Psychosen. Von FRIEDRICH MAUZ. Leipzig: Georg Thieme. 1930. S. 121. Price Rm. 7.50.

In these prognostic studies the influence of Kretschmer is predominant. There is a brief historical introduction in which the author traces the development since Kraepelin of psychiatric thought about the endogenous psychoses finishing with Kretschmer's formulation of the problem as to how far heterogenous mixtures of constitution influence the form and course of the psychosis. His own investigations were carried out between 1923 and 1928, and represent in the main an attempt to answer this question. The bulk of his cases were schizophrenic—1,050 out of a total 1,470. The observations were of necessity not all made by the author, which is a disadvantage. His diagnostic criteria are those of conservative German writers; in his views of schizophrenia he follows the Berze-Gruhle presentation. On the whole he finds more prognostic significance in the habitus and diathetic proportion of the "affect-psychoses" than with schizophrenia, though in all the endogenous psychoses he considers that pyknic build and "fresh" cyclothymic premorbid temperament suggest a favourable outcome. The necessity for taking all the data into consideration is made clear, and penny-in-the-slot prognosis receives short shrift. The work is clearly written and touches on many interesting points, especially of classification.

Social Control of the Mentally Deficient. By S. P. DAVIES. London: Constable. 1930. Pp. 389. Price 13s.

The importance of the social aspects of mental deficiency needs no stressing nowadays; the present work is a valuable contribution in this field. After a review of the measures adopted for the care and training of the feeble-minded since the time of Itard, the eugenic problem is taken up and the case for sterilization examined with temperate caution. The "social indictment" against the defective is shown to be overdrawn, and the more or less controllable factors which lead to antisocial behaviour are demonstrated. Where through special institutions, colonies and community supervision, socializing influences of a beneficent kind are operative, a large proportion of the feeble-minded cease to be social liabilities; the author brings evidence to show that they become social

assets, but to this many would demur. The negation of good doctrines, however, is found in a quotation," rather vivid and perhaps extreme," from Pitkin, in which the advantage and even desirability of a population of morons is supported, inasmuch as they are better fitted to our industrial civilization, more contented and healthy, than people of high intelligence.

The author points out the inadequacy of intelligence testing, used alone, and gives a convincing exposition of the social criteria of deficiency. Many widespread errors are disposed of. The book fully covers the ground which its title suggests; it is written with obvious enthusiasm and much knowledge.

Reflex Action. By F. Fearing. Pp. 350. London: Baillière, Tindall and Cox. 1930. Price 30s.

This volume, which is particularly interesting from the historical aspect, has been written by a psychologist as a study in the development of physiological psychology, but he does not attempt to present the reflex as the explanation of all the activities of the brain or mind, or to treat the subject only as a contribution to the history of psychology.

After an introductory chapter on the conception of voluntary and involuntary action of the Greek physicians and through the Middle Ages, he comes to Descartes, who in his description of animal automatism first recognized clearly that many of our activities are of a nature that would be now called reflex. The work of the early experimentalists is shortly reviewed, and the author then brings us to the more interesting speculations and experiments of the eighteenth century, in which Croone, Whytt, Hartley, Blane, the Monros and other Englishmen took a large share. The work of Bell, Magendie, Marshall Hall, Flourens, Müller and others in the nineteenth century leads directly to the modern conception of reflexes, of the laws that control and integrate them, and the recognition of their fundamental importance in the activity of the body.

The investigations of Sherrington, Magnus and Pavlov are described, and finally the significance of the physiological conception of the reflex to various trends of psychology is considered.

The volume is well written, accurate as far as it can be controlled and unbiased in the presentation of facts and of the theories of the past. It contains much interesting information on the evolution of neurology and physiology.

Aphasia in Children. By Alex W. G. Ewing, M.A., Ph.D. Oxford University Press: Humphrey Milford. 1930. Pp. 152. Price 10s. 6d.

The literature of aphasia is enormous, but the subject of Dr. Ewing's valuable study has hitherto received very little attention. His painstaking investigations were into the apparent aphasia of children, in some of whom he found that the development of normal speech had been hindered by a

remarkable form of partial deafness. The recognition of this lack of auditory acuity for sounds of higher vibration frequency was made possible by skilful and ingenious methods of examination, which are described in detail. Other children whom he investigated showed a congenital linguistic retardation different in kind from the aphasic disturbances of adults.

The book contains a valuable discovery and will be of great interest to otologists and to those concerned with the development of speech. In method of presentation it is admirable.

Die Hypophyse. Von A. EISELBERB, O. HIRSCH, O. MARBURG, J. NOVAK, M. SGALITZER und E. A. SPIEGEL. Berlin: Urban und Schwarzenberg. 1930. S. 66. Price Rm. 3.50.

A year ago the Vienna Society of Medicine and Children's Diseases devoted a meeting to a discussion on the physiology and diseases of the hypophysis, and six of the contributions to this discussion are printed in this volume, which is therefore a valuable compilation of the state of our present knowledge of this subject. Spiegel deals with the anatomy and physiology of the pituitary, and especially with its functional relations with the tuber cinereum: Marburg describes in detail the clinical symptoms of hypophyseal diseases, mainly of tumours; Eiselberg and Hirsch write separately on the operative treatment of pituitary growths by the trans-sphenoidal route; Sgalitzer discusses the radiological therapy of tumours, and Novak the relations of the hypophysis to the sexual organs. The last paper, which is illustrated by photomicrographs, contains an interesting résumé of recent experimental work of this subject.

There is probably no other source in which such a complete and critical review of the physiology and diseases of the hypophysis can be found within the same space.

Étude sur les Narcolepsies. ALICE KYRIAGO-ROQUES. Paris: N. Maloine. 1930. P. 195.

Following the modern French tendency, the author deals with narcolepsy as a symptom due to some structural lesion or disease though it is not always possible to demonstrate it, rather than as a clinical entity. Consequently we find descriptions of narcolepsy as a complication of various organic and functional diseases of the nervous system and of disorders of the endocrine organs. Associated lesions have been most frequently demonstrated in the neighbourhood of the third ventricle and in the anterior part of the midbrain.

The nature of normal and pathological sleep is discussed in early chapters, and some recent experiments on the nervous mechanisms concerned in it are described. The histories of nine patients suffering with narcolepsy are published, and a very full and useful bibliography of the subject is included. Although the monograph adds little to our knowledge of narcolepsy, it will be a useful compilation to those interested in it.

Der Kopfschmerz und seine Behandlung. Von E. POLLAK. Leipzig und Wien: F. Deuticke. 1929. S. 158. Price Rm. 9.

As the recognition of the more common causes and the treatment of headache are the authors' aims, theoretical considerations as the causation and the origin of the pain in various conditions are reduced to a minimum. It is interesting, however, to find that the author believes the sympathetic nerve-fibres in the walls of the blood-vessels of the brain play a large part, and that the headaches which occur in association with disturbances of the circulation, intoxications and metabolic disorders are due to excitation or irritation of these fibres. The treatment of the subject is essentially practical; headaches are grouped according to their apparent cause, and the distinguishing features of each group and the most successful methods of treating them are described concisely and clearly. The book is evidently the work of an experienced clinician and will prove particularly useful to the practitioner and student.

Neuropsyche und Hirnrinde. Von N. E. ISCHLONDSKY. Berlin: Urban und Schwazenberg. 1930. Band I, pp. 328, price Rm. 20. Band II, pp. 356, price Rm. 22.

The first volume of this ambitious work is concerned with the conditioned reflex and its significance in biology, medicine, psychology and pedagogics. Dr. Ischlondsky claims for this study that it is a purely scientific discipline dealing only with measurable data and free from any trace of subjective concepts and speculative psychological tendencies. The investigations in this field have been carried out almost exclusively in Russia, and this book is a useful summary of the work of many physiologists, not elsewhere accessible.

In the second volume the conclusions about the activity of the nervous system are applied to the study of human behaviour. In the title, "Physiological Foundations of Depth Psychology, with especial reference to Psycho-analysis," the author's object is clear. How far he attains it is another matter. His enthusiasm is boundless; he says, for example, that the dynamics of the cerebral cortex during creative mental activity, the mechanism of consecutive and exact as well as of irrational thinking, of memory and will and moral conduct, the essential nature of culture and many more such hard problems are now for the first time completely solved; it becomes evident in reading the book that the claim is exaggerated. Many readers, however, will be stimulated by this bold attempt to clear up all the dark places by the application of a new point of view.

Psychopathology. By J. ERNEST NICOLE. London: Baillière, Tindall and Cox. 1930. Pp. xii + 203. Price 10s. 6d.

The first half of this book is intended to be a guide to the various schools of thought in psychology and psychiatry. The author is better at exposition than at critical appraisal; and many obscure and pretentious writers receive

undeserved or disproportionate attention. The exposition, however, is clear and correct and covers a great deal of ground; naturally it does not pretend to be complete. Dr. Nicole appears to have limited himself to works available in English, if one may judge from the bibliography: this may account for his failure to refer to much recent work in Germany on the psychopathology of schizophrenia, and to do justice to some French and Swiss writers; there is, for example, no reference at all to the views of von Monakow, or of Mignard, Berze or Jaspers, and much of Janet's work is overlooked. Nevertheless, the author has read widely; some 500 books are listed in the bibliography.

In the second part of the book three essays are given. The first on "The Concept of the Ego in Psychiatry," and the third on "Psychopathology and the Herd Instinct," are lucid and interesting. The second on "Type Psychology" is poor; it is based on Jung's types and is rich in generalizations. The difficulties of writing such a book are great; Dr. Nicole has, however, successfully compressed much diverse material into a readable and coherent form.

Modern Psychotherapy. By EMANUEL MILLER. London: Jonathan Cape. 1930. Pp. 131. Price 5s.

Of all branches of medicine, there is none in which treatment is more dependent on theory than in psychiatry. This is especially true of that section of psychiatric practice that is concerned with the "minor psychoses" or neuroses. The divergent theories and the associated modes of treatment are described in this little book clearly and fairly, so that the general practitioner and the student, for whom the book is designed, can learn their main features without being deterred by verbiage and jargon or misled by the author's bias.

The analytic methods of Freud, Jung and Adler, suggestion in its various forms, and persuasion are described. There is a chapter on early treatment and prevention in which the difficult child and the person in the early stages of insanity are considered. A useful glossary of special terms is appended.

The scope of the book is necessarily limited by its size and purpose; the author disclaims any attempt at detailed exposition or critical analysis; the book is, therefore, compact and readable and not likely to give a false impression of finality.

INDEX

TO

BRAIN:

A JOURNAL OF NEUROLOGY,

FOR

VOL. LIII, 1930.

INDEX OF AUTHORS.

PAGE

Allen, I. M.
Tumours of the occipital lobe 194

Allison, S.
Disseminated sclerosis 391

Carmichael, E. A., and Wells, A. Q.
Microglia 1

Cobb, S., and Schaltenbrand, G.
Studies on cats without neocortex 449

Critchley, M.
Anterior cerebral artery and its syndromes 120

Critchley, M., and Greenfield, J. G.
Spinal symptoms in chloroma and leukæmia 11

Croll, M. M., and Eaves, E. C.
The pituitary and hypothalamic region in chronic epidemic encephalitis.. .. 56

Eaves, E. C.
Diabetes insipidus 47

Eaves, E. C., and Croll, M. M.
The pituitary and hypothalamic region in chronic epidemic encephalitis.. .. 53

Finland, M., and Merritt, H.
Vascular lesions of the hind-brain 290

Foerster, O., and Penfield, W.
Structural basis of traumatic epilepsy and results of radical operation 99

Fulton, J. F., Liddell, E. G. T., and Rioch, D. McK.
Influence of destruction of the vestibular nuclei upon posture and the knee-jerk .. 327

Fulton, J. F., Liddell, E. G. T., and Rioch, D. McK.
Influence of experimental lesions of the spinal cord upon the knee-jerk 311

Garland, H. G., and Russell, W. R.
Progressive hypertrophic polyneuritis 376

PAGE

Greenfield, J. G., and Critchley, M.
Spinal symptoms in chloroma and leukæmia 11

Grünbaum, A. A.
Pointing position of the hand as a pathological and primitive reflex 267

Hyland, H. H., and Russell, W. R.
Chronic progressive polyneuritis 278

Kernohan, J. W., and Learmonth, J. R.
Tumour of Gasserian ganglion 86

Kubie, L. S.
Excitation waves which move in closed circuits 166

Langworthy, O. R., and Richter, C. P.
Influence of efferent cerebral pathways upon the sympathetic nervous system .. 178

Learmonth, J. R., and Kernohan, J. W.
Tumour of Gasserian ganglion 86

Liddell, E. G. T., Fulton, J. F., and Rioch, D. McK.
Influence of destruction of the vestibular nuclei upon posture and the knee-jerk .. 327

Liddell, E. G. T., Fulton, J. F., and Rioch, D. McK.
Influence of experimental lesions of the spinal cord upon the knee-jerk 311

Merritt, H., and Finland, M.
Vascular lesions of the hind-brain 290

Moersch, F. P.
Nervous and mental phenomena in paroxysmal tachycardia 244

Paine, C. G., and Yates, A. G.
Arteriovenous aneurysm within the brain 38

Penfield, W., and Foerster, O.
Structural basis of traumatic epilepsy and results of radical operation 99

Pritchard, E. A. B.
Central mechanism of the reflex arc 431

Pritchard, E. A. B.
Electromyogram of voluntary movements 344

Richter, C. P.
Experimental diabetes insipidus 76

Richter, C. P., and Langworthy, O. R.
Influence of efferent cerebral pathways upon the sympathetic nervous system .. 178

Rioch, D. McK., Fulton, J. F., and Liddell, E. G. T.
Influence of destruction of the vestibular nuclei upon posture and the knee-jerk .. 327

Rioch, D. McK., Fulton, J. F., and Liddell, E. G. T.
Influence of experimental lesions of the spinal cord upon the knee-jerk 311

Russell, W. R., and Garland, H. G.
Progressive hypertrophic polyneuritis.. 376

Russell, W. R., and Hyland, H. H.
Chronic progressive polyneuritis 278

Schaltenbrand, G., and Cobb, S.
Studies on cats without neocortex 449

Schmidt, M.
Intracranial aneurysms 489

Seddons, H. J. PAGE
Hæmophilia as a cause of lesions in the nervous system 306

Wells, A. Q., and Carmichael, E. A.
Microglia 1

Yates, A. G., and Payne, C. G.
Arteriovenous aneurysm within the brain 38

INDEX OF SUBJECTS.

Aneurysm, arteriovenous, within the brain. A. G. Yates and C. G. Paine 38
Aneurysms, intracranial. M. Schmidt 489
Anterior cerebral artery and its syndromes. M. Critchley 120
Chloroma and leukæmia, spinal symptoms in. M. Critchley and J. G. Greenfield .. 11
Closed circuits, excitation waves which move in. S. Kubie 166
Diabetes insipidus. E. C. Eaves 47
Diabetes insipidus, experimental. C. P. Richter 76
Disseminated sclerosis. R. S. Allison 391
Electromyogram of voluntary movements. E. A. B. Pritchard 344
Epidemic encephalitis, the pituitary and hypothalamic region in chronic. E. C. Eaves and M. M. Croll 56
Epilepsy, traumatic, structural basis of, and results of operation. O. Foerster and W. Penfield 99
Gasserian ganglion, tumour of. J. R. Learmonth and J. W. Kernohan 86
Hæmophilia as a cause of lesions in the nervous system. H. J. Seddons .. 306
Knee-jerk, influence of destruction of the vestibular nuclei upon posture and the. J. F. Fulton, E. G. T. Liddell and D. McK. Rioch 327
Knee-jerk, influence of experimental lesions of the spinal cord upon the. J. F. Fulton, E. G. T. Liddell and D. McK. Rioch 311
Leukæmia and chloroma, spinal symptoms in. M. Critchley and J. G. Greenfield 11
Microglia. A. Q. Wells and E. A. Carmichael 1
Movements, voluntary, electromyogram of. E. A. B. Pritchard 344
Neocortex, studies on cats without. G. Schaltenbrand and S. Cobb 449
Occipital lobe, tumours of. I. M. Allen 194
Paroxysmal tachycardia, nervous and mental phenomena in. F. P. Moersch .. 244
Pointing position of the hand as a pathological and primitive reflex. A. A. Grünbaum 267
Polyneuritis, chronic progressive. H. H. Hyland and W. R. Russell 278
Polyneuritis, progressive hypertrophic. W. R. Russell and H. G. Garland 376
Posture, influence of destruction of vestibular nuclei on, and the knee-jerk. J. F. Fulton, E. G. T. Liddell and D. McK. Rioch 327
Reflex arc, central mechanism of. E. A. B. Pritchard 431
Reflex, pointing position of the hand as a pathological and primitive. A. A. Grünbaum 267
Sympathetic nervous system, influence of efferent cerebral pathways upon the. O. R. Langworthy and C. P. Richter 178
Tumour of Gasserian ganglion. J. R. Learmonth and J. W. Kernohan 86
Tumours of the occipital lobe. I. M. Allen 194
Vascular lesions of the hind-brain. H. Merritt and M. Finland 290

INDEX OF NOTICES OF BOOKS.

INDEX OF AUTHORS.

PAGE

Babonneix, L.
Syphilis héréditaire du système nerveux 542

Barkman, A.
Syndromes moteurs et réflexes de la paroi abdominale et d'origine cérébrale .. 95

Bertrand, I.
Techniques histologiques de neuropathologie 542

Buhler, K.
Mental development of the child 387

Bumke, O.
Handbuch der Geisteskrankheiten 96, 262, 543

Bumke, O.
Lehrbuch der Geisteskrankheiten 263

Crichton-Miller, H.
Insomnia 263

Crouzon, O.
Études sur les maladies familiales nerveuses et dystrophiques 93

Davies, S. P.
Social control of the mentally deficient 544

Dide, M., et Giraud, P.
Psychiatrie du Médecin-Praticien 265

Dumas, G.
Nouveau traité de psychologie 386

Eckstein, A.
Encephalitis im Kindesalters 259

Eiselberg, A.
Die Hypophyse 546

Ewing, A. W. G.
Aphasia in children 545

Fearing, F.
Reflex action 545

Foerster, O.
Die traumatischen Lasionen des Rückenmarkes 92

Fribourg-Blanc, A., et Rodiet, A.
La folie et la guerre de 1914-1918 264

PAGE

Friedenwald, J.
Pathology of the eye 261

Frostig, J.
Das schizophrene Denken 97

Fuchs-Kamp, A.
Lebensschicksal und Persönlichkeit ehemaliger Fürsorgezöglinge 262

Giraud, P., et Dide, M.
Psychiatrie du Médecin-Praticien 265

Goldflam, S.
Die diagnostische Bedeutung das Rossolimoschen Reflexes 541

Guillain, G.
Études neurologiques 543

Hart, B.
Psychology of insanity 387

Hirsch, O.
Die Hypophyse 546

Ischlondsky, N. E.
Neuropsyche und Hirnrinde 547

Jaensch, E. R.
Eidetic imagery and typological methods of investigation 388

Jakob, A.
Spezielle Histopathologie des Grossbirns 260

Jonesco-Sisesti, N.
Tumeurs médullaires associées à un processus syringomyélique 259

Kretschmer, E.
Medizinische Psychologie 387

Kuntz, A.
Autonomic nervous system 94

Kyriago-Roques, A.
Les narcolepsies 546

Layani, F.
Les acrocyanoses 92

Marburg, O.
Die Hypophyse 546

Marburg, O. und Sgalitzer, M.
Die Röntgenbehandlung der Nervenkrankheiten 543

Marcuse, H.
Die psychischen Reaktionsformen 97

Mauz, F.
Die Prognostik der endogenen Psychosen 544

Miller, E.
Modern psychotherapy 548

Mollaret, P.
La maladie de Friedreich 94

PAGE

Money-Kyrle, R.
The meaning of sacrifice 261

Morel, F.
Hyperostose frontale interne 95

Nathan, M.
Manuel élémentaire de psychiatrie 263

Negus, V. E.
Mechanism of the larynx 93

Nicole, J. E.
Psychopathology 547

Novak, J.
Die Hypophyse 546

Paulhan, F.
Laws of feeling 388

Piéron, H.
Le développement mental et l'intelligence 266

Pollak, E.
Kopfschmerz und seine Behandlung 547

Rodiet, A., et Fribourg-Blanc, A.
La folie et la guerre de 1914-1918 264

Schmidt, M.
Körperbau und Geisteskrankheit 264

Schneider, C.
Die Psychologie der Schizophrenen 98

Sgalitzer, M.
Die Hypophyse 546

Sgalitzer, M., und Marburg, O.
Die Röntgenbehandlung der Nervenkrankheiten 543

Speranski, W. N.
Innere Sekretion und psychische Prozesse 265

Spielger, E. A.
Die Hypophyse 546

Spielmeyer, W.
Teknik der Mieroskopischen Untersuchung des Nervensystems 385

Straus, E.
Geschehnis und Erlebnis 262

Thurzo, E. von.
Ueber einige neuere diagnostische und therapeutische Verfahren 260

Tracy, E. A.
The Basis of epilepsy 387

Zand, N.
Les plexus choroïdes 385

INDEX OF SUBJECTS.

PAGE

Aphasia. Aphasia in children. A. W. G. Ewing 545
Autonomic nervous system. A. Kuntz 94
Child, mental development of. K. Buhler 387
Choroid plexus. Les plexus choroïdes. N. Zand 385
Cortex, cerebral. Neuropsyche und Hirnrinde. N. E. Ischlondsky 547
Deficiency, mental. Social control of the mentally deficient. S. P. Davies .. 544
Encephalitis. Encephalitis im Kindesalters. A. Eckstein 259
Epilepsy, basis of. E. A. Tracy 387
Eye, pathology of. J. Friedenwald 261
Familial diseases. Études sur les maladies familiales nerveuses et dystrophiques. O. Crouzon 93
Feeling, laws of. F. Paulhan 388
Friedreich's disease. La maladie de Friedreich. P. Mollaret 94
Headache. Kopfschmerz und seine Behandlung. E. Pollak 547
Hypophysis. Die Hypophyse. A. Eiselberg, O. Hirsch, O. Marburg, J. Novak, M. Sgalitzer and E. A. Spiegel 546
Insanity, psychology of. B. Hart 387
Insomnia. H. Crichton-Miller 263
Larynx, mechanism of. V. E. Negus 93
Mental deficiency. Social control of the mentally deficient. S. P. Davies 544
Mental development of the child. K. Buhler 387
Narcolepsy. Les narcolepsies. A. Kyriago-Roques 546
Nervous system, autonomic. A. Kuntz 94
Neurology. Études neurologiques. G. Guillain 543
Neurology. Lewandowsky's Handbuch der Neurologie: Die traumatischen Lasionen des Rückenmarkes. O. Foerster 92
Neurology. Réflexes de la paroi abdominale et d'origine cérébrale. A. Barkman .. 95
Neurology. Ueber einige neuere diagnostische und therapeutische Verfahren. E. von Thurzo 260
Pathology of the eye. J. Friedenwald 261
Pathology. Spezielle Histopathologie des Grosshirns. A. Jakob 260
Pathology. Techniques histologiques de neuropathologie. I. Bertrand 542
Pathology. Teknik der Microskopischen Untersuchung des Nervensystems. W. Spielmeyer 385
Psychiatry. Das schizophrene Denken. J. Frostig 97
Psychiatry. Die Prognostik der endogenen Psychosen. F. Mauz 544
Psychiatry. Die psychischen Reaktionsformen. H. Marcuse 97
Psychiatry. Die Psychologie der Schizophrenen. C. Schneider 98
Psychiatry. La folie et la guerre de 1914-1918. A Rodiet, et A. Fribourg-Blanc .. 264
Psychiatry. Geschehnis und Erlebnis. E. Straus 262
Psychiatry. Handbuch der Geisteskrankheiten. O. Bumke 96, 262, 543
Psychiatry. Innere Sekretion und psychische Prozesse. W. N. Speranski 265
Psychiatry. Körperbau und Geisteskrankheit. M. Schmidt 264
Psychiatry. Lebensschicksal und Persönlichkeit ehemaliger Fürsorgezöglinge. A. Fuchs-Kamp 262
Psychiatry. Lehrbuch der Geisteskrankheiten. O. Bumke 263
Psychiatry. Manuel élémentaire de Psychiatrie. M. Nathan 263
Psychiatry. Psychiatrie du Médecin-Praticien. M. Dide et P. Giraud 265
Psychology. Eidetic imagery and topological methods of investigation. E. R. Jaensch 388
Psychology. Le développement mental et l'intelligence. H. Piéron 266

PAGE

Psychology. Medizinische Psychologie. E. Kretschmer 387
Psychology. Nouveau traité de psychologie. G. Dumas 386
Psychology of insanity. B. Hart 387
Psychopathology. J. E. Nicole 547
Psychotherapy, Modern. E. Miller 518
Reflex Action. F. Fearing 545
Reflexes. Die diagnostische Bedeutung des Rossolimoschen Reflexes. S. Goldflam .. 541
Reflexes. Syndromes moteurs et réflexes de la paroi abdominale et d'origine cérébrale. A. Barkman 95
Sacrifice, Meaning of. R. Money-Kyrle 261
Skull. Hyperostose frontale interne. F. Morel 95
Syphilis, nervous. Syphilis héréditaire du système nerveux. L. Babonneix .. 542
Syringomyelia. Tumeurs médullaires associées à un processus syringomyélique. N. Jonesco-Sisesti 259
Treatment. Die Röntgenbehandlung der Nervenkrankheiten. O. Marburg und M. Sgalitzer 543
Vasomotor neurosis. Les acrocyanoses. F. Layani 92

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.